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CLINICAL STUDY - PATIENT STUDY

End of life issues in brain tumor patients

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Abstract Despite aggressive antitumor treatment, the prognosis of brain tumor (BT) patients remains poor. In the last stage of disease, BT patients present severe symptoms due to the growing tumor or to treatment side-effects, which require adequate palliative management and supportive therapy. However, studies specifically addressing palliative care and end-of-life (EoL) issues in BT patients are lacking. This study explores symptoms experienced by BT patients in the last weeks of disease and EoL issues observed in a population of brain tumor patients followed at home until death by a neuro-oncological home care palliative unit set up in our Institution in 2000. From October 2000 to December 2005, 324 patients affected by brain tumor and discharged from our Institution were enrolled in a comprehensive program of neuro-oncological home care supported by the Regional Health System. Out of 324 patients enrolled in the home care program, 260 patients died of which 169 (65%) were assisted at home until the end of life and have been included in this study. Clinical symptoms, palliative treatments and EoL treatment decisions were collected from home clinical records. Among the 169 patients assisted at home until death, the most frequent symptoms observed in the last four weeks of life were: epilepsy 30%, headache 36%, drowsiness 85%, dysphagia 85%, death rattle 12%, agitation and delirium 15%. Palliative management of brain tumor patients requires a multidisciplinary approach performed by a well trained neuro-oncology team. Development of home care models of assistance may represent an alternative to in-hospital care for the management of patients dying of brain tumor and may improve the quality of end-of-life care.

Keywords Palliative care · End of life treatment decisions · Brain tumor

Introduction

Despite aggressive antitumor treatment, the prognosis of brain tumor (BT) patients remains poor. Survival of malignant gliomas is less than 1 year for glioblastoma and 24–36 months for anaplastic astrocytoma. In the last stage of disease, BT patients present severe symptoms due to the growing tumor or to treatment side-effects, which require adequate palliative management and supportive therapy [1, 2]. Increasing attention has been focused on the need to improve quality of care at the end-of-life in cancer patients and existing data suggest that too many patients do not receive adequate palliative care in the last stage of disease [3, 4]. A recent European study, the EurELD study, evaluating EoL decision making in six European countries, revealed that only 40% of competent patients are involved in end-of-life medical decisions; fewer than 7% express their wishes in advance and more than 50% of decisions are made without involving the patients or their families [5]. EoL issues in neuro-oncology concern the decisions relating to medical treatment, including nutrition and hydration of patients in coma, withholding of steroid treatment and palliative sedation [6]. The process of treatment decision making in the terminal stage of brain tumor patients is

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often complicated by the presence of cognitive problems that may affect patients' competence to express treatment preferences. The complex care needs of BT patients and their families in advanced stages of disease should be managed by well trained multidisciplinary teams [7, 8]. However, studies specifically addressing palliative care and EoL issues in BT patients are lacking. A better knowledge of clinical and ethical issues could help to improve the educational training and quality of care of neuro-oncology services [9].

This study explores symptoms experienced by BT patients in the last weeks of disease and the EoL issues observed in a population of brain tumor patients followed at home until death by a neuro-oncologic home care palliative unit activated in our Institution in 2000. Clinical symptoms, palliative treatments and EoL treatment decisions were collected from home clinical records.

Patients and methods

From October 2000 to December 2005, 324 patients affected by brain tumor and discharged from our Institution were enrolled in a comprehensive program of neuro-oncological home care supported by the Regional Health System. All patients received neurological assistance, nursing, psycho-social support and rehabilitation at home [10]. The aims of this assistance model are to provide continuity in care between the hospital and the local health system, to meet the patients' needs of care in every stage of disease, to support the families and to reduce the re-hospitalization rate. Home staff includes one neurologist, five nurses, one psychologist, two rehabilitation therapists, one social worker. The management of patients at home is discussed by home staff in weekly meetings and coordinated by the Neuro-Oncologic Centre at the Regina Elena Cancer Institute. Intensity of care depends on the different phases of disease and usually is considered "high" after hospital discharge, "low" during follow-up, "medium" in the phase of recurrence or progression and "very high" in the last stage of disease. Clinical data of patients assisted at home are collected in a home clinical record filled at every home access. In order to evaluate the prevalence of symptoms in the last stage of disease, the home clinical records of patients were retrospectively analysed. Clinical symptoms, palliative treatments and EoL treatment decisions were collected.

Results

Out of 324 patients enrolled in the home care program, 260 patients died of which 169 (65%) were assisted at home until the end of life and have been included in this study. Table 1 describes the characteristic of patients in study: 135 were affected by malignant gliomas, 30 by cerebral metastases from solid tumors and four by other histology (Two CNS lymphoma, one germinoma, one medulloblastoma). Among the 169 patients assisted at home until death most frequent symptoms observed in the last four weeks of life were: epilepsy 30%, headache 36%, drowsiness 85%, dysphagia 85%, death rattle 12%, agitation and delirium 15% (Table 2).

Table 1 Characteristics of patients

N	169
Sex	M 82; F 87
Age (average)	56 (15–93)
Hystology	
GBM	135
Brain metastases	30
Others CSN primary tumors	4

Table 2 Incidence of symptoms in the in the last month of life in 169 patients death for brain tumor

Epilepsy	30%
Headache	36%
Dysphagia	85%
Death rattle	12%
Drowsiness	85%
Agitation and delirium	15%
Steroid-induced adverse effects:	
Hyperglicemia	10%
Psycosis	4%

Epilepsy

Seizures occurred in 51 patients (30%) in the last four weeks before death and were partial in 85% and generalized in 15% of cases. Six percent of patients presented repeated seizures or status epilepticus. Incidence of seizures was higher in gliomas respect patients with brain metastases (34% vs. 10%, respectively). Most patients (53%) who had seizures in the last months of life had experienced seizures in the past and were on treatment with antiepileptic drugs (AEDs); in 24 cases (47%) seizures occurred in patients who had not presented epilepsy in the past (14 assuming prophylactic AEDs; 10 without AEDs). Seizure management near the end of life requires a specific approach: considering that patients may present difficulties in swallowing oral medications, oral AEDs have to be substituted with intramuscular anticonvulsants (Phenobarbital). In case of repeated seizures or epileptic status, patients were treated with i.v. lorazepam [11, 12].

Headache

Thirty-six percent of patients presented pain. In the large majority of patients, headache was mild, intermittent, due to increased intracranial pressure, and usually responded to steroid treatment. In some cases, headache was severe and required a high dosage of steroids and pain medication with non-opioids pain relief or opioids.

In patients with meningeal syndrome due to meningeal involvement, both for neoplastic meningitis from systemic cancer (Seven cases) and for meningeal spread from brain oligodendroglioma (Two cases), pain treatment required a multidrug approach with steroids, opioids and gabapentin.

In some cases, neuropathic pain may originate from cranial nerve involvement: in two cases in our population, we observed atypical cranial headache responding to indometacin due to cavernous sinus infiltration in a patient with meningeal carcinomatosis and facial pain in trigeminal ophthalmic branch in a patients with a brain stem progressive low grade glioma.

Dysphagia

Eighty-five percent of our patients presented dysphagia in the last four weeks of life. The median time interval between dysphagia onset and death was 21 days (range: 8–60). Loss of the ability to swallow may induce pulmonary inhalation and may affect nutrition and hydration. Moreover, the patients' difficulty in the oral intake of drugs, liquids and food requires appropriate modification of treatment, the training of caregivers in nutrition, and early discussion with families and the home care team of end-of-life treatment decisions concerning nutrition and hydration. In all our patients presenting dysphagia in the last weeks of life, anticonvulsant treatment was changed with the substitution of oral drugs with intramuscular barbiturates.

Consciousness deterioration

Most of our patients showed a progressive loss of consciousness in the last weeks of life and entered into deep coma in the last days in 82% of cases. Lethargy, confusion and night-day reversal may be early symptoms of consciousness deterioration. Cognitive impairments are the result of multiple factors and may be managed by increasing antiedema treatments. However, the presence of delirium or behavioural disturbances may alter the usual "peaceful" pattern of dying.

The incidence of pain in the last hours of life is difficult to assess, but the presence of agitation and restlessness with moaning and grimacing is often interpreted as physical pain and requires appropriate treatment.

Fifteen percent of our patients presented agitation, delirium and confusion without a complete loss of consciousness. In 21 cases, bad symptom control required the use of pharmacologic sedation (neuroleptic, opioids and benzodiazepine) [13], but in some cases agitation may be controlled by reducing steroid dosage. Patient agitation and delirium in the last hours of life can be very distressing for family members, particularly in the home care setting.

Death rattle

Changes in breathing patterns are the rule in the last hours of life of BT patients and usually occur in unconscious dying patients. In some cases, difficulty in clearing upper airways leads to an accumulation of respiratory tract secretions. Death rattle may be very distressing for the family and home care professionals, and occurred in 12% of our patients. Anticholinergic drugs reduce the production of secretion and mild dehydration may help to control this symptom.

End-of-life decision making process

End-of-life decisions (EoL) concern the treatment decisions that may prolong or reduce life. Considering brain tumor patients, EoL treatment decisions concern no-treatment decisions: withdrawal of supportive treatment (steroid, anticonvulsant), withdrawing–withholding of artificial nutrition-hydration in patients in prolonged vegetative state and palliative sedation. Figure 1 describes the most important treatment decisions concerning nutrition, hydration and, in some cases, palliative sedation taken in our patients.

The decision making process involved patient's relatives and the home care team. Adequate information concerning treatments and symptom control strategies were given with the aim of sharing decision-making process. Families were

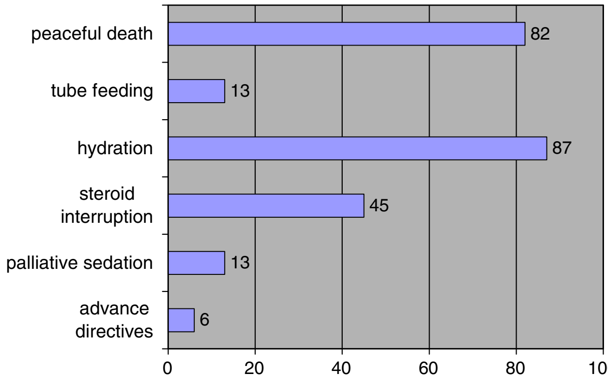

Fig. 1 End of life treatment decisions in 169 brain tumor patients who died at home (Values in %). Home Care Unit, Regina Elena Cancer Institute, Rome

informed that parenteral feeding does not alter patients' survival and may induce an increase in secretions and brain oedema. The large majority of patients included in this study did not express advance directives and were not competent to make treatment decisions in the last month of life; only 6% of patients declared early directives about end-of-life treatment. Patients' awareness about prognosis was evaluated by psychologist (LG) and registered in home clinical record: only 52.9% of our patients were fully aware about prognosis while 27% was defined partially aware and 20% unaware. Most patients (87%) received only mild hydration with intravenous fluid administration (500–1,000 ml/day) while 13% received tube feeding requested by the patient's family. Patients presenting bad symptom control with an agitated death required the use of pharmacologic sedation. Intravenous benzodiazepines and neuroleptics were administered with the aim of reducing the patient's suffering in 13% of cases, after discussion with patients' families. In patients presenting progressive consciousness deterioration and not responding to treatment, steroid dosage was slowly tapered (45% of patients). Steroid tapering was planned after discussion with family and dose was progressively reduced. Usually, a small dose was maintained to avoid adrenal failure. However, 82% of patients presented a peaceful death with a progressive loss of consciousness and good symptom control not requiring pharmacologic sedation.

Discussion

The quality of end-of-life care delivered to patients dying of cancer is a major public health concern [14]. There is a large consensus on the need to improve the quality of care of neuro-oncologic patients. Neuro-oncologists devote most of their efforts to seeking active treatment against the tumor, while dedicating very little time to what happens to patients who have progressive disease and whose treatment has ended [3]. The main goals of EoL care are to offer BT patients adequate symptom control, to avoid inappropriate prolongation of dying and to provide psycho-social support for the patient and family. However, currently there is a lack of palliative care provision for patients affected by advanced brain tumor.

Although the limits of a retrospective approach, the present study represents the first description of the symptoms and care needs observed in a large population of brain tumor patients at the end of life.

In our population of BT patients, we observed a high incidence of distressing symptoms that may influence the process of dying. In order to allow the patient to experience a peaceful death, control of pain, confusion, agitation, delirium or seizures requires specific palliative interventions performed by well trained neuro-oncological teams. The high frequency of dysphagia (85%) in the last days of life reported in our study emphasizes the importance of defining the correct management of specific issues such as nutrition and hydration in BT patients more precisely.

The literature shows that even when patients are competent, it is rare that they or their families are involved in the decisions [5].

Moreover, communication with BT patients is particularly difficult since the rapid evolution of neurological symptoms can affect cognitive functions. The observational evidence available [15] suggests that BT patients' awareness of their prognosis varies considerably and that up to 40% are unaware of it. Not all patients seem to wish to be completely informed about their prognosis and the communication of bad news should be tailored to the coping styles of the individual patients and relatives.

Considering that the large majority of brain tumor patients lose the competence to participate in a shared decision making process, it is of outstanding importance to plan treatment decisions about nutrition and hydration, discussing them with families and with patients, when it is possible. The aim is to obtain a consensus between all participants on withholding-withdrawing decisions, respecting patients' and families' values. As the "shared decision" taken together by physicians, nurses, and the patient's family may be the best approach to end-of-life decisions, common guidelines are needed.

In summary, palliative management of brain tumor patients at the end of life requires a multidisciplinary approach performed by a well trained neuro-oncology team.

Nevertheless, there is a great need for education in palliative care and end-of-life care for brain tumor. Wider availability of palliative programmes and home care models of assistance may represent an alternative to in-hospital care for the management of patients dying of brain tumor and may improve the quality of end-of-life care.

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References

1. Batchelor TT, Byrne TN (2006) Supportive care of brain tumor patients. Hematol Oncol Clin North Am 20(6):1337–1361. doi:10.1016/j.hoc.2006.09.013
2. Taillibert S, Delattre JY (2005) Palliative care in patients with brain metastases. Curr Opin Oncol 17(6):588–592. doi:10.1097/01.cco.0000183673.15133.e2
3. Taillibert S, Laigle-Donadey F, Sanson M (2004) Palliative care in patients with primary brain tumors. Curr Opin Oncol 16(6):587–592. doi:10.1097/01.cco.0000142075.75591.02
4. Voltz R, Borasio GD (1997) Palliative therapy in the terminal stage of neurological disease. J Neurol 244(Suppl 4):S2–S10. doi:10.1007/PL00007721

5. Bosshard G, Nilstun T, Bilsen J et al (2005) Forgoing treatment at the end of life in six European countries. Arch Intern Med 165:401–407. doi:10.1001/archinte.165.4.401
6. Faithfull S, Cook K, Lucas C (2005) Palliative care of patients with a primary malignant brain tumor: case review of service use and support provided. Palliat Med 19(7):545–550. doi:10.1191/0269216305pm1068oa
7. Junck L (2004) Supportive management in neuro-oncology: opportunities for patient care, teaching and research. Curr Opin Neurol 17:649–653. doi:10.1097/00019052-200412000-00003
8. Pruitt AA (2005) Treatment of medical complications in patients with brain tumor. Curr Treat Opin Neurol 7:323–336
9. Carver AC, Vickrey BG, Bernat JL et al (1999) End-of-life care: a survey of US neurologists' attitudes, behaviour and knowledge. Neurology 53:284–293
10. Pace A, Parisi C, Di Lelio M et al (2007) Rehabilitation in brain tumor patients. J Exp Clin canc Res 26(3):297–300
11. Krouwer HGJ, Pallagi JL, Graves NM (2000) Management of seizures in brain tumor patients at the end of life. J Palliat Med 3(4):465–475. doi:10.1089/jpm.2000.3.4.465
12. Glantz MJ, Cole BF, Forsyth PA et al (2000) Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Neurology 54:1886–1893
13. Bonito V, Caraceni A, Borghi L et al (2005) The clinical and ethical appropriateness of sedation in palliative neurologic treatment. Neurol Sci 26:370–385. doi:10.1007/s10072-005-0503-9
14. Earle CC, Ayanan JZ (2006) Looking back from death: the value of retrospective studies of end of life care. J Clin Oncol 24(6):838–840. doi:10.1200/JCO.2005.03.9388
15. Davies E, Higginson IJ (2003) Communication, information and support for adults with malignant cerebral glioma: a systematic literature review. Support Care Cancer 11:21–29