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Brain metastases from stomach cancer – The role of different treatment modalities and efficacy of palliative radiotherapy



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ABSTRACT

Aim: To evaluate different treatment modalities, sequences, and prognostic factors in patients with brain metastases from stomach cancer.

Background: Brain metastases from gastric cancer are rare and late manifestation of the disease, occurring in less than 1% of gastric cancer patients. The prognosis is poor and median overall survival is 1.3–2.4 months. The standard treatment scheme has not yet been described. Most studies present small sample sizes. The choice of treatment scheme is individually based on performance status, number, location and size of metastases, the status of primary tumor and the presence of other metastases.

Materials and methods: Sixteen patients diagnosed with brain metastases from gastric cancer in Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch.

Patients, mostly men (69%) aged 51–75 years, (median 68.5 years). Thirteen (81.25%) had treatment of primary tumor before diagnosis of brain metastases. Primary metastatic gastric cancer was diagnosed in 6 patients (37.5%), in 3 cases (18.75%) brain was the site of those metastases. Treatment schemes were individually based.

Results: We identified prognostic factors influencing OS: performance status, number of brain metastases, type of treatment. Median OS was 2.8 months. Median time to brain metastases was 12.3 months and it was shorter in patients with pretreatment metastases to other organs. Patients treated with combined treatment had median survival of 12.3 months.

Conclusions: Aggressive treatment schemes are needed to improve the outcome. Prognostic factors such as performance status, number of metastases, dissemination to other organs are helpful in considering the best treatment options.

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1. Background

Stomach cancer is the third most common cause of cancer-related deaths worldwide (740,000 of deaths per year) after lung and breast cancer. The treatment results remain unsatisfactory. Over 30% of patients at the time of diagnosis is in advanced stages of the disease presenting with metastases mostly to the liver, lung or bones. Brain metastases from stomach cancer are uncommon, being diagnosed in 0.47–0.7% of patients; therefore, the standard treatment has not yet been established.^{1–3}

Patients with brain metastases from gastrointestinal tract have generally poorer prognosis than patients with brain metastases from other cancers, for example breast or lung, where median survival is 2 months and 7 months, respectively.^{2,4}

The symptoms of brain metastases are typical: headache, weakness, altered mental status, focal neurological deficits, gait or visual disturbances, ataxia. Sometimes brain metastases are asymptomatic.

There are several treatment modalities, and the choice of treatment scheme depends on the number and location of brain metastases, the presence of metastatic disease in other organs, the status of primary tumor site, and patient's performance status. In most cases the aim of treating metastases of any location is not to destroy all cancer cells, but to achieve an appropriate relief of symptoms and assure good quality of life.^{5–7}

Surgery or stereotactic radiosurgery (SRS) and additional whole brain radiotherapy (WBRT) can be used in patients in good performance status and good prognosis (expected overall survival of 3 months or more), with up to three brain metastases. SRS is a very precise technique that delivers usually a single dose to a well-defined intracranial target with protection of normal surrounding brain tissue. It is a non-invasive method of radiotherapy resembling surgery but without perioperative complications.

SRS can be used for treating rather small tumors (up to 3 cm) and when there are up to three tumors in the brain, it can be also considered as a radiation boost to resection cavity.^{6–9}

When the metastases are multiple, patients in good general condition are irradiated using whole brain radiotherapy. In patients in poor general condition, if the expected survival is less than 3 months and the brain metastases are multiple and inoperable, steroids and best supportive care can be used.⁸

The role of chemotherapy and radiosensitizers in the treatment of brain metastases remains undefined mostly because of the blood–brain barrier. WBRT can destroy blood–brain barrier, and consequently facilitate the penetration of cytostatic drugs to the brain tumor.

Brain metastases from stomach cancer are usually late manifestation of the disease and patients are often in severe cachexia and in bad performance status. Modern palliative chemotherapy and immunotherapy lengthen survival by a few months, and possibly the frequency of brain metastases from stomach cancer will rise; therefore, radiotherapy becomes an important treatment modality.

It is known that prognostic factors such as KPS, age, extracranial disease and primary tumor status are useful to

choose a tailored strategy of treatment. Other factors, such as number, size, location of intracranial metastases, histology, interval between primary tumor diagnosis and detection of brain disease are also considered.⁷

2. Aim

There are few literature studies concerning treatment and prognostic factors in patients with brain metastases from stomach cancer; therefore, the authors decided to evaluate the efficacy of palliative radiotherapy, to describe different treatment modalities and sequences, and to analyze prognostic factors in this group of patients.

3. Materials and methods

Between 2002 and 2011, a total of 16 patients were diagnosed with brain metastases from stomach cancer at Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Gliwice. The data of all the patients were collected and retrospectively analyzed. The patients ranged in age from 51 to 75 years (median 68.5 years). There were 11 men (69%) and 5 women (31%). All patients had histologically verified gastric cancer. Metastatic gastric cancer was diagnosed during the first clinical examination tests in 6 patients (37.5%), and in half of the patients (18.75%) these were metastases to the brain. The detailed characteristics of patients are presented in [Table 1](#).

Of the 16 patients, 9 (56.25%) underwent primary radical surgery after diagnosis of stomach cancer by biopsy. Four patients (25%) underwent palliative chemotherapy; in 1 case palliative gastrectomy was performed, in 2 cases (12.5%) chemotherapy was added to palliative radiotherapy. Three patients (18.75%) were not treated before diagnosis of brain metastases.

Brain metastases were diagnosed by magnetic resonance imaging (MRI), or contrast-enhanced computed tomography (CT). Having been diagnosed, the patients were proposed with several treatment options according to their prognostic factors. Three main treatment modalities were local, i.e. surgery and radiosurgery or whole brain radiotherapy. They could be used in different sequences.

In WBRT, two opposite fields techniques were used to deliver 20 Gy in 5 fractions with 6 MV photons to the whole brain while sparing critical organs, such as the lenses.

After WBRT, one or two fractions of stereotactic radiosurgery were delivered if patient met the criteria, i.e. regression of metastases to 3 cm of diameter or/and complete regression of some of multiple metastases to a total number of up to three tumors. SRS dose was individually defined based on patient's performance status and tumor volume or technical possibilities that are restricted by critical organs proximity (optic nerves, optic nerves chiasma, brain stem, internal ear).

Areas of incomplete regression were treated with 12–20 Gy in one or two fractions. Stereotactic radiosurgery was used after neurosurgery if there was a tumor mass left or as a boost to the resection cavity. Treated region was relatively small; therefore, the dose could be escalated to 20 Gy using 6 MV photons. The treatment regimens are presented in [Table 2](#).

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