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# Dissemination of malignant gliomas beyond the central nervous system

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## Summary

**Background**

Gliomas are the most frequently diagnosed primary intracranial tumours in adults. This group incorporates astrocytomas, oligodendrogliomas and ependymomas. Glioma treatment in adults usually means surgery and radiotherapy, and in the case of poorly differentiated tumours, chemotherapy may also be applied. Failures in the treatment of malignant gliomas are mostly local recurrences, intracranial dissemination and, very seldom, metastases beyond the central nervous system

**Aim**

The aim of this paper was to present two instances of extraneural dissemination in cases of malignant glioma of the brain.

**Materials/Methods**

Two patients with dissemination of malignant glioma were diagnosed and treated in our department during the last 20 years.

**Results**

Treatment effects were poor.

**Conclusions**

Extraneural brain tumour dissemination is infrequent and their treatment remains an unsolved problem. Treatment is similar to that of primary glioma, especially in cases with high dynamics.

Neither chemotherapy nor radiotherapy are able to produce even a short term palliative effect.

**Key words**

**brain tumour • malignant glioma • dissemination of malignant gliomas**

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## BACKGROUND

Gliomas are the most frequently diagnosed primary intracranial tumours in adults [1]. This group incorporates astrocytomas, oligodendrogliomas and ependymomas [2–5]. Glioma treatment in adults usually means surgery and radiotherapy, and in the case of poorly differentiated tumours, chemotherapy may also be applied [6]. Failures in the treatment of malignant gliomas are mostly local recurrences, intracranial dissemination and, very seldom, metastases beyond the central nervous system [6,7]. To date there are over 100 cases of extraneural metastases in cases of malignant glioma described in the literature [6,7]. Most commonly, extraneural dissemination occurs in young patients aged between 30 and 50 years. Metastases are most frequently identified in the following organs: bone marrow, lungs and pleura, lymph nodes, liver, retroperitoneal space and cardiac muscle [6–9]. Glioblastoma multiforme may spread by means of the cerebrospinal fluid. This occurs in 0.4–0.5% of all patients with neuroectodermal tumours, most frequently in gliosarcomas [6]. Choucair [9] reports that extraneural dissemination was diagnosed in 0.1% of 72 patients with malignant gliomas. Abbott, quoted by Karen Fink [6], maintains that surgical intervention causes infiltration of glioma cells into the venous system owing to reduced intracranial pressure. She reported that, on the basis of the literature, one can say that there are approximately 79 documented cases of malignant glioma with extraneural metastases. Among those patients were 68 adults and 11 children. Denier and colleagues [10] described two cases of metastatic glioblastoma metastases involving the lungs, kidneys, liver and bones. Liwnicz and Rubinstein [11] reported that ependymomas constitute about 6.2% of all gliomas, but that cases of extraneural metastasis among these tumours constitutes around 16.4% of all glioma metastases. They wrote that 5% of patients with gliomas suffered from oligodendrogliomas, and 5.2% had metastases arising from oligodendrogliomas.

## AIM

The aim of this paper was to present two instances of extraneural dissemination in cases of malignant glioma of the brain.

## MATERIALS AND METHODS

Between the years 1983 and 2002, 1465 adult patients were treated for intracranial tumours in

the Radiotherapy Department of the Provincial Oncology Hospital in Opole. Among them were 965 patients with malignant gliomas. Within this group we diagnosed two cases of extraneural dissemination.

## Case study 1

A female patient, AK, aged 28, underwent partial removal of a brain tumour in May 1987. The tumour was located in the right temporal region. Histopathological diagnosis was: fibrillary astrocytoma partly gemistocytic, partly anaplastic. The patient was irradiated and received doses of 40Gy to the whole brain and 20Gy to the tumour bed, in combination with chemotherapy as follows: Lomustine 120mg/m<sup>2</sup> every 6 weeks. The first dose of Lomustine – 120mg/m<sup>2</sup> – was administered on the first day of irradiation. In total 5 doses of Lomustine were given. 3 months after completion of chemotherapy, the patient developed a painful and rapidly growing tumour in the right mandible area with accompanying lockjaw. The patient was operated. Observations at the time of operation were of a tumour reaching from the base of the skull to the lower pharynx and extending into the right parapharyngeal and paraspindylous areas. The histopathological diagnosis was of a malignant tumour of neurogenic origin. A comparison specimens from the intracranial and parapharyngeal areas showed that this was the same tumour. Subsequently, the patient was irradiated twice a day, receiving 72Gy from a Co-60-unit and a 10MeV electron beam. Following irradiation, chemotherapy commenced. This consisted of Lomustine 120mg/m<sup>2</sup> every 6 weeks and Cis-platinum 50mg/m<sup>2</sup> on days 1–3 every 4 weeks. The patient underwent 4 chemotherapy cycles. After a further 6 months, a hard painful infiltration, 6×4cm, appeared in the right preauricular area and the patient developed a fever of up to 39°C. Also, abdominal pains developed. The pains were concentrated in the lumbar region where massive oedema developed, involving the lower right leg, the groin and the right iliac fossa. A pathological examination of material collected from the right groin infiltration showed a malignant tumour of neurogenic origin, anaplastic glioma. 14Gy irradiation was administered, though the treatment was interrupted owing to a high fever and a rapid deterioration in the patient's general condition. The patient died the following month, 7 months after the diagnosis of dissemination.

## Case study 2

A male patient JŚ, aged 46, was admitted to the Provincial Oncology Hospital in October 2001 following surgery to a tumour of the brain in the left frontal region. An postoperative examination of material revealed a malignant tumour of sarcomatous structure, probably gliosarcoma – a mesodermal and ectodermal tumour of complex texture. The patient qualified for combined radiotherapy and chemotherapy. Chemotherapy: PCV program: Lomustine 120mg/m<sup>2</sup> + Procarbazine 100mg/m<sup>2</sup> for 14 days + Vincristine 1mg per week for 3 successive weeks, every 6 weeks. The patient was irradiated using a 9MV photon beam, receiving 60Gy to the tumour bed over 6 weeks. In total, the patient underwent 5 chemotherapy cycles. One month later, the patient complained of coughing, and his temperature rose to 38°C. Examination revealed a regrowth of the tumour at the tumour bed. 2<sup>nd</sup> stage chemotherapy commenced as follows; Vepesid 100mg/day orally for 10 days, every 2 weeks and Endoxan 100mg/day orally for 10 days, every 4 weeks. A chest X-ray revealed widespread mottling in both lung fields, especially in the upper and central lobes. Lesions were round and of various size, merging in places. Bronchoscopy revealed no abnormalities, though cytological examination of the pleural effusion showed numerous malignant cells of neurogenic origin. An ultrasound scan of the abdominal cavity showed an oval tumour in the area of the hilus measuring 35×24mm. The patient died in December 2002, 2 months after the diagnosis of dissemination.

## DISCUSSION

According to the literature, the majority of cases of malignant glioma with dissemination beyond the central nervous system were associated with very rapid spread to many organs, and this process was very aggressive in nature [8–10]. Often, in cases where dissemination was found, the patient was febrile suggesting transmission by both blood and lymph vessels [9,10]. Both of the patients described above had a fever and the course of dissemination was very violent. In 1980 Pasquier [8] reported finding 72 cases of malignant gliomas with extraneural metastases. Among these, 59.7% were metastases to the lungs and pleura, 51.4% to the lymph nodes, 30.5% to the bones, and 22.2% were metastases to the liver. Among metastases to the lymph nodes, 62% of cases were metastases to the cervical nodes and 32% were metastases to the pulmonary hilus nodes. In patient AK, described above, dissemination was to

many lymph node groups while in patient JŚ it was to the lungs and pleura. Our observations are thus concordant with the observations of the authors quoted. According to Liwnicz and Rubinstein, all patients with dissemination had suffered local recurrence [11]. In our material, patient AK had no local recurrence, though a quickly growing local recurrence was found in patient JŚ. Brain glioma with dissemination beyond the central nervous system usually reduces survival time [7–10]. Numerous authors suggest irradiation and chemotherapy [9] for the treatment of extraneural dissemination. This however represents only a palliative or symptomatic treatment and, according to Fink and Schold [6], the best way to prevent malignant glioma from metastasising beyond the central nervous system is to properly and effectively treat the primary tumour. The cases we have presented here were treated chemically, and by irradiation, from the moment that dissemination was diagnosed. The treatment was of a palliative nature and we observed very short lived effects of therapy (amounting to several weeks) only in patient AK.

## CONCLUSIONS

Extraneural brain tumour dissemination is infrequent and their treatment remains an unsolved problem. Treatment is similar to that of primary glioma, especially in cases with high dynamics.

Neither chemotherapy nor radiotherapy are able to produce even a short term palliative effect.

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