Original Article

ADJUVANT TREATMENT OF BRAIN ASTROCYTOMAS II DEGREE WITH DESFERAL: A PRELIMINARY REPORT

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Summary

Median postoperative survival of patients with brain astrocytomas II degree has stayed unchanged for the past several decades, and is still a therapeutic challenge. Since February 1, 1995 the author has been applying Desferal in adjuvant treatment of 28 patients with brain astrocytomas II degree. Fourteen of the patients have survived for more than five years. All the patients treated are alive and clinically stable. Computer tomography (CT) and nuclear magnetic resonance (NMR) have shown no further growth of the rest of the tumours. Desferal is an effective medicine for adjuvant treatment of brain astrocytomas II degree.

Key words: brain astrocytomas II degree, adjuvant treatment, Desferal

Introduction

Surgical treatment of brain astrocytomas II degree is restricted by the localization of the tumour, and total resection is rarely possible. Patients usually receive adjuvant therapy. During the last decades, this combined treatment has not significantly changed the postoperative survival (Table 1) [3, 4, 9, 10]. That is the reason to seek new ways and means for treatment of these tumours.
Table 1.

Patients and Methods

Since February 1, 1995 we have used Desferal for adjuvant treatment of brain astrocytomas II degree. The choice of this pharmaceutical agent is linked to our investigations of aluminium. We found that it was significantly augmented in the blood serum of the patients with brain gliomas [7]. The same element was twice as low in the tumour tissue collected intraoperatively, as compared to its content in the surrounding white brain matter [8].

We started treating and continue to treat 28 patients. All of them are alive as of April 1, 2008 and have shown no signs of progress of the disease. In this article we present the first 14 patients, who have already reached the 5-year postoperative survival. Data of these patients

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are on Table 2.

Desferal was developed for withdrawal of iron in some haematological diseases. In 1976, A. C. Alfrey et al. shared their good achievements in chelation of aluminium with Desferal in dialysed patients, an important medical problem at that time [1, 2].

To treat brain astrocytomas II degree, we use a specific scheme. Treatment is introduced soon after the operation, and is eventually combined with another adjuvant treatment. During the first six months, we apply Desferal in a daily dose of 0.5g intramuscularly for three consecutive days a week. Every six months the intervals between the three-day courses are increased in the following manner: one course per two weeks, then per three weeks, per one month, two months and then per three months. Finally, we recommend that the three-day treatment is administered twice a year.

Table 1. Five-years postoperative survival of patients with cerebral astrocytomas II degree

Authors	Year	Number of patients	Survival in %
Ph. Philipov	1986	33	36%
J. Shinoda et al.	1998	33	66%
F. W. Kreth et al.	2006	239	56%
M. Law et al.	2006	35	46%

Table 2. Postoperative survival of the patients with astrocytomas II degree

№	Sex	Age	Localization of the tumour	Volume of the resection	Total radiotherapy in Gy	Hemo-therapy	Survival in years
1	male	53	Right frontal	partial	56	-	13.2
2	male	46	Right temporal	partial	60	-	11.8
3	female	29	Left parieto-temporal	biopsy	-	-	10.8
4	male	56	Right temporo-occipital	partial	60	-	9.2
5	male	56	Right temporal	partial	60	-	8.9
6	male	20	Right temporal	subtotal	60	-	8.8
7	male	34	Right temporal	partial	60	-	7.8
8	male	39	Right frontal	partial	60	-	7.4
9	male	39	Right temporal	partial	60	-	7.3
10	female	63	Left frontal	partial	58	-	7.2
11	female	47	Left frontal	partial	60	-	6.8
12	female	50	Right temporal	partial	60	-	6.8
13	male	21	Bifrontal	biopsy	60	CCNU 6x320 mg	6.5
14	Male	35	Bifrontal	partial	60	-	5.9

Results

The longest survival in the treated group is 13.2 years at present. All the patients are clinically stable. Of the 14 patients with a longer than 5-year survival, two are employed in agriculture, two are economists, one woman specializes in economics and another is a tailor. There is also an active computer specialist. The rest of the patients are busy in their households. Periodical CT and NMR check-ups have revealed no progress in the rest of the tumours. No side effects were observed.

Discussion

Adjuvant treatment with Desferal undoubtedly prolongs the life of patients with brain astrocytomas II degree. We also had some success in treating 21 patients with brain astrocytomas III and IV degree. Their postoperative survival was nearly twice as long as compared to that of the control group [9].

In 1981, we began to use active non-specific immunotherapy with rabies vaccine in cases of multiform glioblastomas. The results were encouraging - the median postoperative survival was prolonged twice, as compared with the controls [6]. However, treatment with rabies vaccine was not effective in ten patients with low-grade gliomas. Only five of them reached a 5-year postoperative survival.

Nowadays we can only guess at the therapeutic mechanism of Desferal in cases of brain gliomas. Desferal chelates iron and aluminium from the organism of the patients, and iron is an integral part of many enzymes. The Ukranian researchers O. Mykhaylyk et al. revealed hyperferremia in human glial tumours [5]. The positive effect of Desferal in the treatment of gliomas may be considered as a result of iron chelation. On the other hand, an effective role of aluminium in human metabolism has not been proved by contemporary science, though it is suspected.

It is too early to make final conclusions about the treatment of brain astrocytomas II degree with Desferal. However, every neurosurgeon is aware that at least half of the patients with such gliomas develop further tumour malignization, deteriorate and die in the near postoperative years. We did not observe such events in our cases, so the assumption is that treatment with Desferal was useful and could be recommended.

Conclusion

Our preliminary results from adjuvant treatment with Desferal for brain astrocytomas II degree have shown definite therapeutic efficacy.

References

1. Alfrey AC, Le Gendre GR, Kaehny WD. The dialysis encephalopathy syndrome. Possible aluminium intoxication. N Engl Y Med. 1976;294(2):184-8.
2. Channon SM, Arfeen S, Ward MK. Long term accumulation of aluminium in patients with renal failure. Trace Elem Med.1988;5(4):154-7.
3. Kreth FW, Faist M, Grau S, Ostertag CB. Interstitial 125 I radiosurgery of supratentorial De Novo WHO Grade 2 astrocytoma and oligoastrocytoma in adults. Cancer. 2006;106(6):1372-81.
4. Law M, Oh S, Johnson G. Perfusion magnetic resonance imaging predicts patient outcome as an adjuvant to histopathology: a second reference standard in surgical and neurosurgical treatment of low-grade gliomas. Neurosurgery. 2006; 58 (5):1099-107.
5. Myhaylyk O, Dudchenko N, Cherchenko A. Peculiarities of nonheme iron metabolism upon glial brain tumors. Proceedings of the 3rd International symposium on trace elements in human; 2001 Oct 4-6; Athens, Greece. 2001. p. 1100-12.
6. Philipov Ph. An attempt to use rabies vaccine in the treatment of patients with glioblastoma multiforme. Vopr Neurochir. 1988;(3):38-40.
7. Philipov Ph, Tzatchev K. Aluminium concentrations in serum of patients with intracranial tumors. Zentralbl Neurochir. 1993; 54(1):148-50.
8. Philipov Ph, Tzatchev K. Aluminium, manganese, copper and selenium in the neoplastic tissue and white brain matter of patients with intracranial tumors. Proceedings of the 4th International symposium on trace elements in human; 2003 Oct 9-11; Athens, Greece. 2003. p. 430-4.
9. Philipov Ph. Trace elements selenium, manganese, copper and aluminium in patients with intracranial tumors concerning their therapeutic influence [dissertation]. Pleven: Medical University ; 2004.
10. Shinoda J, Sakai N, Nakatani K, Funakoshi T. Prognostic factors in supratentorial WHO grade II adults. Brit J Neurosurg. 1998;12(2):318-24.