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Resection of C6 gliomas in rats with the aid of the waterjet technique

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ABSTRACT

Objectives: While clinically the safety and efficacy of waterjet resection of brain tumors have been shown, evidence that waterjet dissection improves tumor resection radicality in comparison with conventional techniques is still missing. In the present study, resection radicality and tumor-free long-term survival of both techniques were evaluated in a C6-glioma model.
Material and methods: Fifty-thousand C6-glioma cells were stereotactically transplanted in the left frontal lobe of 100 male Sprague-Dawley rats. After MRI-scanning for evaluation of tumor extension, microsurgical tumor resection was performed with conventional techniques (n = 50) or with the waterjet dissector at pressures of 6 bar (n = 50). Twenty-five animals of each group were sacrificed after surgery for histological analysis. For analysis of survival after tumor resection, twenty-five animals of each group were followed-up to analyze tumor-free survival using the Kaplan Meier method.
Results: In the waterjet group, the resection cavity was free of C6-tumor cells in 10/25 (40%) rats showing a trend (p = 0.3) towards better resection radicality compared to the rats that were treated conventionally (7/10; 28%). R1-resection with up to 250C6 cells/object slice was found in 14/25 (56%) rats after waterjet dissection compared to 6/25 (24%) rats treated conventionally showing significance (p < 0.01). Probability of survival was 38% after 2 weeks and 20% after 6 months in the waterjet group compared to 30% and 16% respectively in the conventional group. Diffuse tumor cell spreading with possible influence on survival was shown in 47/50 rats.
Conclusion: In this experimental model, waterjet tumor resection did reveal significantly better resection radicality compared to the conventional technique. Although a direct transfer of these results to human glioma surgery is prohibited, the waterjet technique might contribute to the best possible resection radicality in human gliomas. Nevertheless, tumor cell spreading remains a major problem. Further studies have to address that the surgical results – in deed – improve the postoperative outcome.

1. Introduction

The treatment of gliomas remains a challenge for neurosurgeons and neurooncologists, and, due to their invasive nature, complete resection is not possible. In high-grade gliomas such as anaplastic astrocytoma (AA) or glioblastoma multiforme (GBM) the outcome is still poor [1,2]. Despite progress in the preoperative imaging of the tumor [3–5], the improvement of intraoperative techniques for enhancement of tumor tissue such as 5-aminolevulinic acid (ALA) [6–8], combined postoperative radio- and chemotherapy [9–12], or even novel therapeutic approaches [13], less than half of the glioblastoma patients survive more than one year [1]. Extended tumor resection enhances the length and quality of survival for patients with supratentorial high-grade and low-grade gliomas [14–18]. Today, with the aid of neuronavigation and intraoperative mapping it is even possible to perform radical but safe resection of tumors located at eloquent areas [12,18–20].

In glioma surgery, waterjet resection presents one surgical technique for precise dissection of tumor tissue from the adjacent brain under preservation of even small blood vessels [21–23]. The surgical technique has been used by the authors' group in various intracranial pathologies with a constant expansion of the operative spectrum and good success since 1997 [21–27]. The waterjet dissector consists of a pencil-like handpiece with a nozzle of 120 μm diameter surrounded by a suction device. Its nozzle emits a waterjet with different pressures that can be preset. In general, pressures

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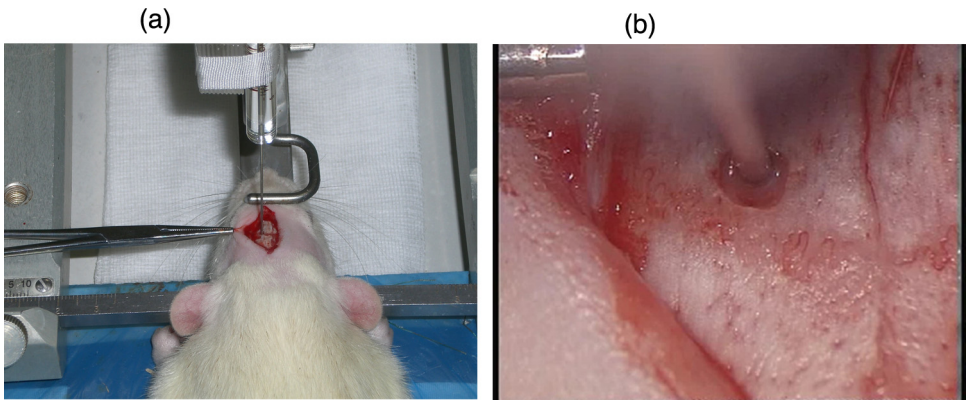

Fig. 1. Left sided burr hole for C6 transplantation located 3 mm lateral the midline and 1 mm anterior to the coronar suture. OP setting (a) and transplantation of C6 cells with a Hamilton syringe (b).

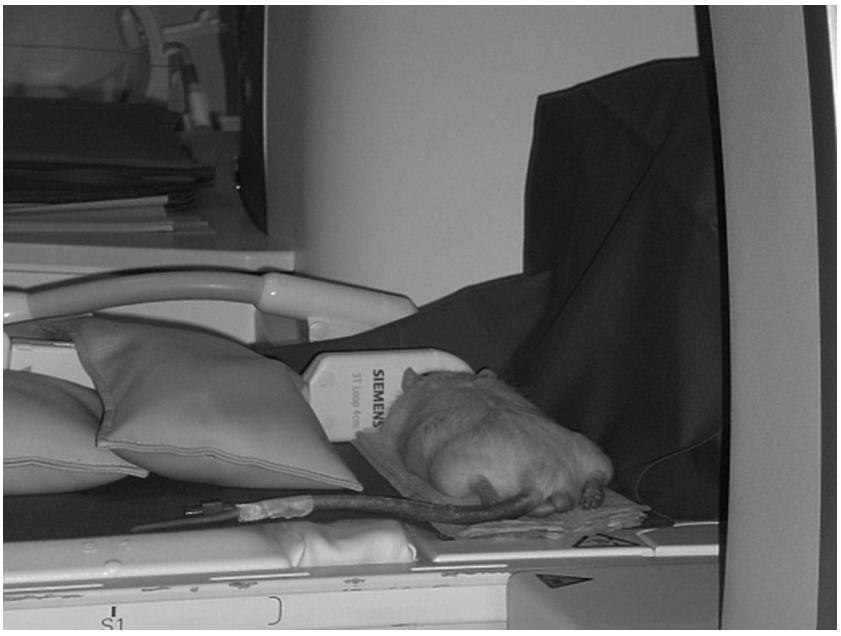

Fig. 2. Position of the rat during MR imaging in the 3 Tesla scanner with its head placed in a finger coil with a diameter of 4 cm.

of 4–10 bar are used in glioma surgery [26,28]. While clinically the safety and efficacy of this technique without a higher risk of complications has been shown [23,25–28], evidence that waterjet dissection improves tumor resection radicality in comparison with conventional techniques is still missing.

In the present study, 100 rats with intracranial C6 gliomas transplanted in the left frontal lobe, were operated on with conventional microsurgical techniques (n = 50) or with application of the waterjet dissection device (n = 50) set at a pressure of 6 bar. In 25 animals of each group, the resection cavity of the rat brains was analyzed histologically with respect of tumor resection radicality. The animals' neurological status was closely observed for neurological deterioration after tumor resection and for the clinical appearance of recurrent tumors. The postoperative time of survival was analyzed in the remaining 25 animals of each group.

2. Materials and methods

All animal procedures have been approved by the institutions' animal care and use committee ad the German State Committee of Laboratory Animal Research.

2.1. C6 glioblastoma cell culture

C6 glioblastoma cells were maintained in monolayer culture (37 °C, 5% CO_2, 95% O_2) in Dulbeccos modified eagle medium (DMEM, Gibco invitrogen™, Germany) containing 10% fetal bovine serum, penicillin and streptomycin (Gibco-BRL®, Germany). Cells were subcultured and used for transplantation when they were in an exponential phase of growth. To harvest, the cells were incubated 4 min with 5% trypsin-EDTA (Gibco invitrogen™, Germany) before adding DMEM to make a single cell suspension. After centrifugating of the suspension at 2000 rpm for 5 min, the medium was removed and the cells were resuspended in DMEM. For determination of the cell concentration, the suspension was given in a counting cell chamber. After counting, the cells were centrifugated again and resuspended with DMEM (without fetal bovine serum and antibiotics) to a final concentration of 10^7 cells ml^{-1}.

2.2. C6 cell transplantation

One-hundred male Sprague-Dawley rats (300–400 g, Charles River, Sulzheim, Germany) were included in this study. The animals were anaesthetized with chloralhydrate (36 mg/kgBW) given