



5-ALA Fluorescence guide removal in high grade glioma: technical observations

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Introduction

Malignant glioma represents a relevant therapeutic issue and the value of extensive surgical resection remains debated; recent evidence suggests that radical removal is associated with better survival. An interesting tool for identifying tumor tissue and increasing the extent of surgery is represented by fluorescence-guided resection, taking advantage of metabolic and structural changes induced by a natural precursor of heme biosynthetic pathway, 5-amino-levulinic acid (ALA), which accumulates electively in tumor cells. A randomized controlled, multicenter phase III trial of malignant gliomas revealed that 5-ALA fluorescence-guided surgery led to a higher rate of complete resection of the contrast enhanced tumor and improved progression-free survival compared with the control group [1].

References

1. Stummer W, Pichlmeier U, Meinel T, Wiestler OD, Zanella F, Reulen HJ. Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. Lancet Oncol. 2006; 7(5):392-401

Methods

54 patients were operated on using fluorescence guided tumor resection. Preoperatively, all enrolled patients had MRI showing contrast enhancing lesions (fig. 1a). MRI within 72 hours after surgery (fig. 1b) and thereafter at 3-month interval was performed. 32 patients were newly diagnosed tumour, 22 were recurrent malignant glioma. An oral dose of 20 mg 5-ALA /kg body weight was administered to each patient. By a NC4 OPMI Pentero operating microscope (Zeiss), enabled switching from xenon light (fig. 1c) to violet-blue light (440 nm) for visualizing fluorescence (fig. 1d), the 5-ALA fluorescence surgical resection was performed. Histology was in 48 glioblastoma (1 gliosarcoma), in 4 anaplastic oligodendroglioma, in 1 oligodendroglioma I WHO and in 1 pleomorphic xanthoastrocytoma. All the patients, as first line treatment, were submitted to radiotherapy and chemotherapy; in recurrent tumors second and in some cases third line treatments were administered. The follow-up ranged from 8 months to 3 years.

Results

In 52/54 cases the red fluorescence due to 5-ALA absorbed by tumor cells was seen: 47 glioblastoma, 4 anaplastic oligodendroglioma and 1 xanthoastrocytoma. Tumor fluorecence was not visible in only 2 cases: one GBM, previously treated with antiangiogenetic drugs and another one hemorrhagic GBM. Specially in recurrent tumors, the fluorescence-guided surgery was helpful to identify, inside the gliotic tissue, some red areas with active tumor from dark perilesional "healthy" brain (fig.1d). In subcortical tumors the 5-ALA fluorecence, added to neuronavigation, provided a valuable guide for initial corticotomy. Furthermore, after surgery no relevant neurological deficit caused by 5-ALA guided resection were observed. No skin disorders were observed. Early postoperative MRI confirmed gross total resection without contrast enhancement in 80 % of patients. In tumors close to eloquent or deep areas removal was subtotal. At the follow-up 24 patients are still alive. Considering overall survival of recurrent gliomas we obtained a median extension of at least 9.0 months.

Case 15: Recurrent GBM

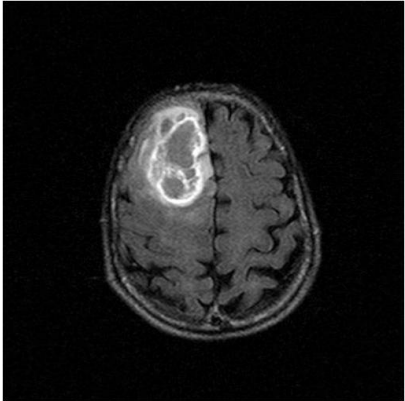


fig.1a) preop MRI

Case 15: Recurrent GBM

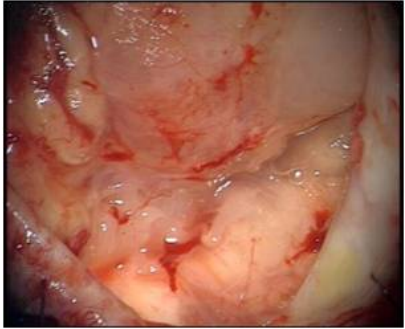


fig. 1c) gliosis by white light

Conclusions

The 5-ALA was helpful to localize the tumor on the cortex and extend resection of infiltrating tumor. Specially in recurrence, it was a guide for orientation in the gliotic scar tissue. Early postoperative MRI confirmed gross total removal. Patients affected by glioblastoma are elctive for this technique. Extended resections by 5-ALA fluorescence guide

Case 15: Recurrent GBM

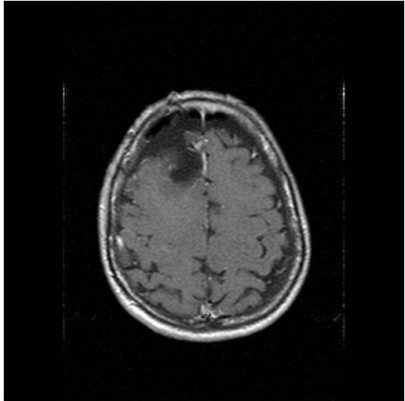


fig. 1b) early postop MRI

Case 15: Recurrent GBM

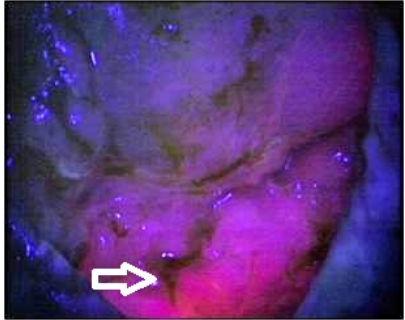


fig.1d) red tumor by blue l.

does not impair neurological functions and can impact on the overall survival of patients affected by malignant glioma.

Learning Objectives

- 1) importance of the fluorecence guide surgery
- 2) discuss on the efficacy of the 5-ALA for tumor infiltrating tissue
- 3) identify the criticism of 5-ALA surgery