Insulin-like growth factor 2 in paediatric gliomas: expression, intracellular localization and association with clinical outcome

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Background

- ✓ The insulin-like growth factors (IGFs) system are known to play an important role in both normal and neoplastic growth.
- ✓ IGF2 overexpression has been identified in several cancers and was significantly related to the initiation and progression of cancers.
- ✓ Gliomas are the most frequent solid tumours in paediatric patients.

Aim

To characterize the expression and intracellular localization of IGF-2 in a large cohort of paediatric gliomas, and its association with clinical outcome.

Methods

- ✓ Design: **Prospective study** of gliomas from paediatric patients that underwent surgery in our Hospital between August 2007 and April 2018 .
- ✓ Gliomas were classified as low (LGG) and high grade (HGG) according to "2016 WHO classification of central nervous system tumours".

Immunohistochemistry (IHC): IGF-2 intracellular expression and localization

- ✓ Using IGF2 antibody (Abcam Ab9574) in fixed tumour samples.
- ✓ Evaluated independently by two pathologists under optic microscope.
- ✓ The results were classified according to IGF2 labeling in:
  - **Negative**
  - **Positive : Cytoplasmatic**
  - **Cytoplasmatic/nuclear**

Quantitation PCR (qPCR) : IGF2 gene expression

- ✓ In those tumours where fresh sample were available.

- ✓ Follow-up since surgery until August 2019.
- ✓ Clinical outcome: - **Dead**
  - **Alive: Without tumour**
  - **With tumour**

Results

Total gliomas studied by IHC	Low grade n= 82
	High grade n= 17
Sex (F/M)	F: 42 / M: 57
Age: medium ± SD (range)	8.24 ± 4.87 years (0.37 – 18.32)
Follow-up: medium ± SD (range)	4.66 ± 2.21 years (0.27 – 11.81)
Gliomas localization	Supratentorial n=48
	Infratentorial n=46
	Intramedullary n=5
Clinical outcome (7 drop-outs)	Alive without tumour n= 32
	Alive with tumour n= 35
	Dead n = 17

Total gliomas studied by qPCR	Low grade n= 37
	High grade n= 9
Sex (F/M)	F: 20 / M: 26
Age: medium ± SD (range)	9.03 ± 4.82 years (0.87 – 18.32)
Follow-up: medium ± SD (range)	5.05 ± 1.43 years (1.65 – 7.22)
Gliomas localization	Supratentorial n=22
	Infratentorial n=23
	Intramedullary n=1
Clinical outcome (5 drop-outs)	Alive without tumour n= 21
	Alive with tumour n= 14
	Dead n = 6

Staining	**n**	**LGG**	**HGG**
Negative	11	10	1
Citoplasmatic	21	16	5
Citoplasmatic and nuclear	66	55	11

No association was found between IGF-2 expression and subcellular localization with tumour grade, neither with clinical outcome

$p > 0,05$ Chi^2 Test

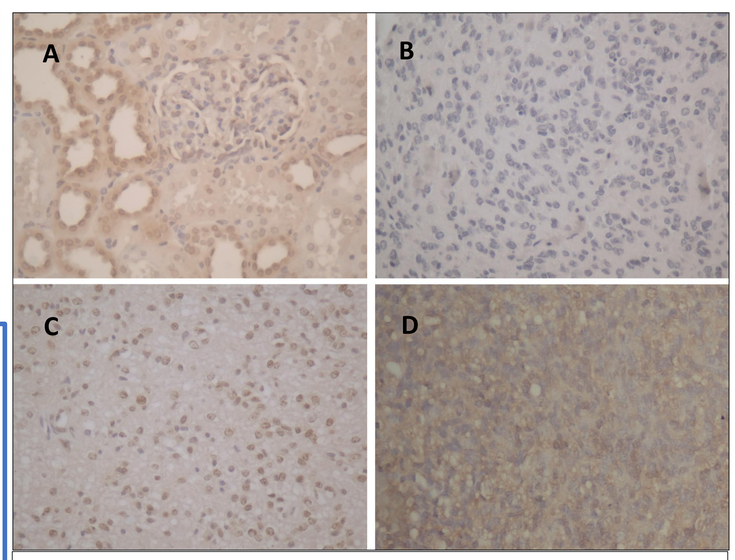
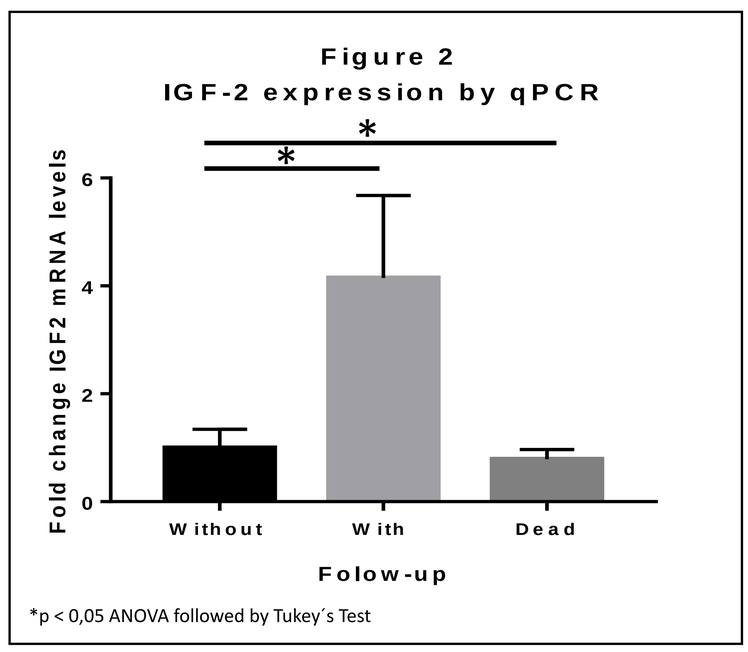


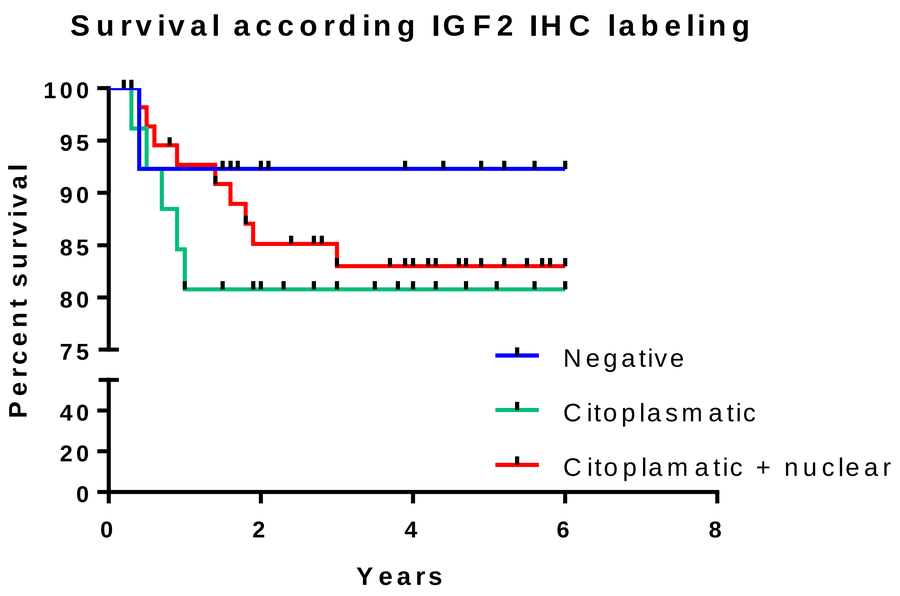
Figure 1. IHC for subcellular localization of IGF2 in paediatric gliomas A : Kidney tissue showing citoplasmatic and nuclear IGF2 labeling (Control) B : Glioma with negative IGF2 staining – C : Glioma showing positive staining in nuclear compartment – D : Glioma showing positive staining in citoplasmatic compartement.



*p < 0,05 ANOVA followed by Tukey´s Test

IGF-2 expression was higher in living patients bearing tumors compared to tumour free or deceased patients, regardless of tumour grade.

This association persisted in low grade tumours while was not found in patient with high grade gliomas.



Conclusions:

- **We are reporting the second tumour type presenting nuclear IGF2 intracellular localization and the first in the paediatric patients.**
- In contrast with results found in other tumours, IGF-2 intracellular localization performed by IHC **does not correlate with clinical outcome** in paediatric gliomas. However, the association between initial elevated IGF-2 mRNA levels with clinical outcome in low grade gliomas suggest a role for IGF2 in the biological behavior of these tumours.