Puberty and pituitary-gonadal axis function after treatment for a childhood brain tumor

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INTRODUCTION

Primary malignant central nervous system (CNS) tumors are the second most common childhood malignancies (21%). Late effects during follow-up, including pituitary-gonadal axis dysfunction and repercussions on puberty and fertility may alter the quality of life of survivors.

AIM

To describe the pituitary-gonadal axis function of patients who were treated for a primary brain tumor more than 5 years ago in order to try to refine the risk factors for the different dysfunction.

METHOD

we included 204 patients diagnosed with a primary brain tumor before 18 years, followed in pediatric endocrinology at the University Hospital "Necker-Enfants Malades" in Paris between January 2010 and December 2015. Data was retrieved from medical records. Untreated gliomas and pituitary adenomas were excluded. Analysis of pituitary-gonadal axis function was made according to tumor type or location (suprasellar – SS or non suprasellar – NSS).

Definitions:

Delayed puberty: absence of pubertal signs (Tanner stage B1 at age 13 in girls or Tanner stage G1 at age 14 in boys), or lack of appropriate progression of puberty (>4 years between first pubertal signs and menarche in girls or the onset and completion of testicular growth in boys).

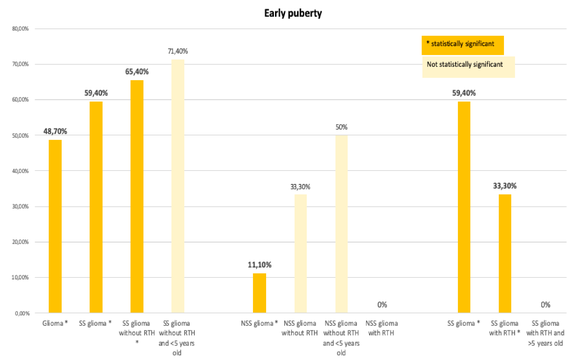
Hypogonadotropic hypogonadism: delayed puberty with low basal LH/FSH/estrogen or testosterone levels corresponding to the children range.

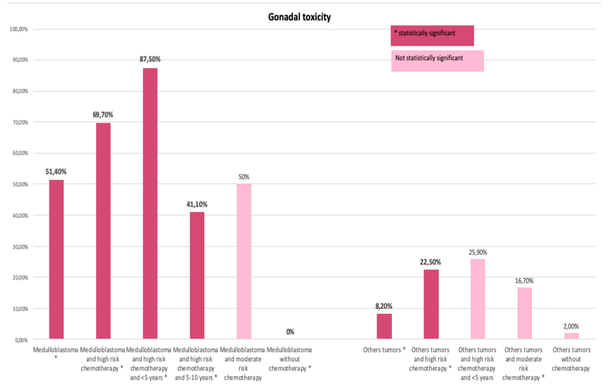
Gonadal toxicity: basal LH or FSH levels above the upper limit of the reference range for the sex (FSH>10 mUI/l for boys and >20 mUI/l for girls) and/or low AMH levels in girls (undetectable) or low inhibin B levels in boys (<80 pg/ml).

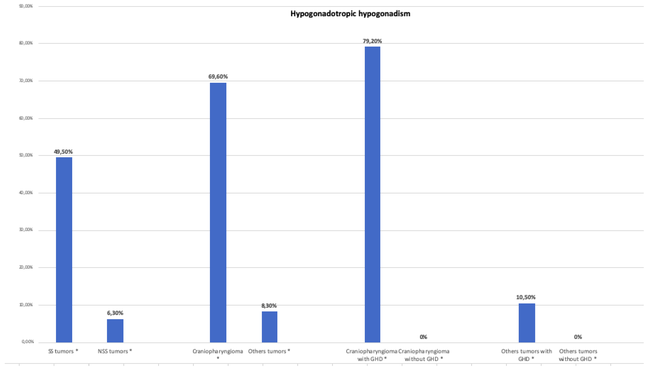
Precocious puberty (PP): pubertal signs appear <8 years in girls, or <9 years in boys. *Early puberty (EP)*: pubertal signs appeared between 8 and 9 years in girls or between 9 and 11 years in boys. In our study, we merged PP and EP into the same group.

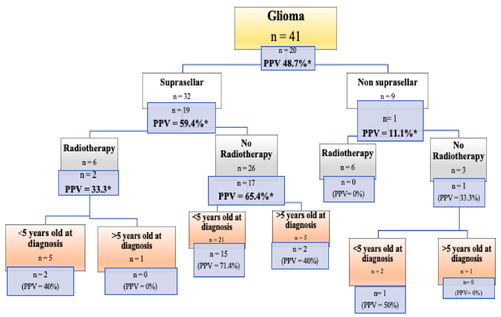
Analyses: When analyzing *the risk of precocious puberty*, we excluded all patients who were, at diagnosis, >9 years for girls and >11 years for boys, with a total of 195 patients. When analyzing *the risk of hypogonadotropic hypogonadism*, girls <13 years and boys <14 years were excluded, as they were not yet old enough for this diagnosis, leaving 187 patients. For *the risk of gonadal toxicity*, all 204 patients were included.

RESULTS

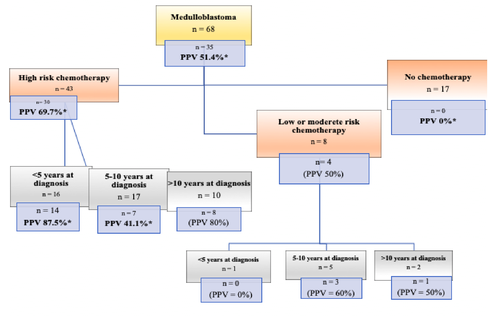




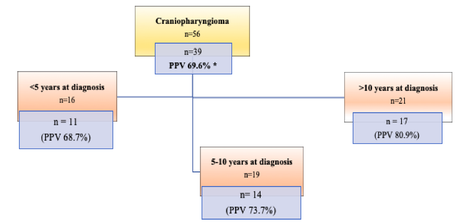




Suprasellar glioma is associated with early puberty in 60% of cases in comparison with 10% in non suprasellar glioma. The higher risk of early puberty is SS glioma treated without radiotherapy (65%) compared those treated with radiotherapy >30Gy (33%). The PPV reach 70% if the patient with SS glioma treated without radiotherapy was <5 years old at diagnosis compared patients with >5 years old at diagnosis (40%).



Medulloblastoma is associated with risk of gonadal toxicity in 70% of cases because of high risk chemotherapy received, and until 87,5% if the patient is <5 years old at diagnosis. The risk is 0% if the patient doesn't receive any chemotherapy and the risk is intermediate if the patient is treated with moderate risk chemotherapy



If no GHD, **PPV 0% *** for hypogonadotropic hypogonadism.
If GHD, **PPV 79.2% ***.

Craniopharyngioma is associated with risk oh hypogonadotropic hypogonadism because of the tumor itself in 70% of cases. There is not risk factor as age, sex or treatment, which increase this PPV. The predictive factor is having GH deficiency with PPV of 80%.

CONCLUSIONS

The type of tumor, its location and treatment are the main factors that guide the risk for pituitary-gonadal axis dysfunction. Awareness concerning potential late effects is essential to guide parental and child information, medical surveillance and adequate and timely hormone replacement therapy.

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