The Endocrine late effects of childhood neuroblastoma therapy: The 20 years’ experience of a single center

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INTRODUCTION

Neuroblastoma is a childhood neoplasia affecting extracranial neuroectodermal tissue and accounting for about 10% of solid childhood malignancies, which represents 1/100,000 children every year. Survival rate approach 70%, leading to the emergence of a population of adult survivors having been exposed to adverse effects of cytotoxic drugs or therapy. Adequate management of late effects require appropriate awareness of them.

- Patients treated for neuroblastoma are exposed to surgery, chemotherapy, radiotherapy or MIBG therapy. All those treatments potentially affect the endocrine and gonadal system.

AIM

Our work consists in a retrospective review of endocrine and gonadal late effects arising in survivors treated for neuroblastoma in childhood.

MATERIAL & METHODS

- We retrospectively reviewed medical files of 80 patients (M/F = 27:23) treated for neuroblastoma between 1994 and 2016.
- Collected data consisted in age, height, and weight at diagnosis and at last follow-up. Standard deviation values were computed for those parameters to enable comparison.
- Biological value such as TSH, BMI at last follow-up and gender were recorded at the time of last follow-up.
- Incidence of late effect in our sample was compared to incidence of late effects due to neuroblastoma therapy in larger series.
- Statistical analysis through ANOVA with repeated measures (STATISTICA Software) were conducted to study impact of chemotherapy on height and weight at follow-up.

RESULTS

- Neuroblastoma are divided as either low or high risk, depending on age at diagnosis, localization, cytogenetic and presence of metastasis. Low-risk neuroblastoma mainly occur in children below 12 months of age and are often managed with surgery only. If localization of tumor makes it inoperable, chemotherapy is used as first line of therapy. High-risk neuroblastoma therapy require chemotherapy, MIBG therapy, radiation therapy, and sometimes autologous hematopoietic stem cell transplant.
- In large follow-up series, late effects of neuroblastoma therapy affect 89% of patients, and endocrine complications affect 82% of female and 45% of males treated for childhood neuroblastoma.

TOXICITY BY THERAPEUTICAL AGENTS

Alkylating agents (carboplatine, cyclophosphamide):
- Ovarian failure
- Testicular dysfunction
- Dental abnormalities
- Lung fibrosis
- Renal impairment and tubulopathies
- Second malignancies (MDS/leukemia, thyroid)

Radiotherapy
- Ovarian failure
- Leydig cell failure
- Growth deficiency and impaired growth (sclerosis)
- Severe dental abnormalities
- Second malignancies (MDS/leukemia, thyroid)

MIBG therapy
- Hypothyroidism (50-80%)
- Second malignancies

Surgery
- Neurological complications

Ovarian failure
- Premature ovarian failure appearing as the main complications.

CONCLUSION

- Treatment for childhood malignancies exposes children to late effects affecting, among other, the endocrine system. In children treated for neuroblastoma, hypothyroidism, gonadal failure and altered growth appear as the main complications. A close follow-up of survivors is thus highly appropriate.

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