Treatment of Children with Medulloblastoma with Craniospinal Radiation Therapy and Chemotherapy.

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علاج الورم الأرومى النخاعى في الأطفال بالعلاج الاشعاعى والعلاج الكيميائى

رسالة مقدمة من الطبيبة
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ماجستير طب الأورام

توطئة للحصول علي درجة الدكتوراه في طب الأورام

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Abstract

Prognosis of children with medulloblastoma is poor especially in cases with incomplete surgical resection of the tumor. Bad outcome of the disease encouraged us to look for a safe and effective way of medulloblastoma treatment that would be able to improve the prognosis for children with high risk medulloblastoma. The current study is undertaken to determine the feasibility of treating children with high risk medulloblastoma who have non-disseminated disease with craniospinal irradiation and chemotherapy , administered during and after radiotherapy. The study is based on the hypothesis that the addition of chemotherapy to radiotherapy will result in improved treatment outcome of high risk medulloblastoma cases

Results of our study have shown that administering six consecutive cycles of cisplatin, etoposide and vincristine with after surgical resection and craniospinal irradiation given concurrently with weekly vincristine is feasible in newly diagnosed patients with high risk incompletely resected pediatric medulloblastoma. The encountered toxicities are not significantly different from craniospinal irradiation alone and addition of adjuvant chemotherapy results in significantly better progression free survival.

Key workds: Pediatric Medulloblstoma, High risk, Radiotherapy, Ajuvant chemotherapy.

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Introduction

The overall incidence of central nervous system (CNS) tumors in children aged 0 to 19 years is 3.9 per 100,000 person-years in the United States (Central Brain tumor Registry of the United States 2002). The most common malignant CNS tumor of childhood is medulloblastoma (MB), with an overall incidence among children aged 0 to 19 years of 0.63 per 100,000 person-years or 16% of all pediatric brain tumors. Of all CNS tumors of childhood, cerebellar tumors make up 18.1%; 40% of these are MB. The peak incidence of medulloblastoma occurs between 3 and 4 years of age. MB in adults is rare, making up only 1% of all CNS tumors (Chan AW et al 2002). The incidence is highest in the age range 20 to 34 at 0.21 per 100,000 person-years and tails off to 0.05 per 100,000 person-years by the age range 55 to 64 before dropping to zero.

Bailey and Cushing first used the term "medulloblastoma" in 1925 to describe a pluripotential embryonic tumor that rose in the cerebellum (Bailey P et al 1925). With a near 100% mortality rate initially, it represented a neurosurgeon's worst nightmare— an aggressive neoplasm located in one of the most challenging sites in a young child, who is almost certain to die from the disease within a matter of months or less. From these stark beginnings, substantial improvement in survival has been made because of a combination of several factors: *(a)* the implementation of radiation therapy to counter the rapid growth of the tumor; *(b)* improvements in neurosurgical equipment and technique

that allowed greater accessibility to the posterior fossa and permitted a greater chance of gross total surgical resection; *(c)* the development of chemotherapy protocols that strive to optimize prevention of recurrence and minimize the chance of metastatic dissemination; and *(d)* the advent of modern cross-sectional imaging techniques, especially magnetic resonance (MR) imaging, that have completely changed the method of assessment for follow-up in affected patients(Kelly K et al 2003).

Tumors are currently risk-stratified as average risk or high risk depending on clinical factors such as age, extent of resection, and presence of metastases. Molecular biology is beginning to improve upon clinical prognostication and may soon provide the means to accurately predict response to therapy. Treatment for average-risk MB has achieved a level of success that allows efforts to be focused on the limitation of adverse treatment effects. Therapy for high-risk and relapsed MB has been positively affected by the advent of chemotherapy . In addition, molecular targets are being elucidated and new therapeutic agents are being tested for safety and efficacy. Treatment for this disease has evolved a great deal over the preceding decades, but a great deal of work remains to be done to effect reliable cures while reducing long-term sequelae of therapy (Brian R et al 2004).

The current study is undertaken to determine the feasibility of treating children with high risk medulloblastoma who have non-disseminated disease with craniospinal irradiation and chemotherapy , administered during and after radiotherapy. The study is

based on the hypothesis that the addition of chemotherapy to radiotherapy will result in improved treatment outcome of high risk medulloblastoma cases. A retrospective arm will be included as a control group and a comparison will be made between the two groups as regards the response to treatment and toxicity.

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