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Letter to Editor Open Access

Metronomic Chemotherapy is a Novel Option for Treating Paediatric Inoperable Brain Tumours in Developing Countries

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Letter to the Editor

Brain tumors are the second common neoplasms in children, after leukemias [1]. Some brain tumors are unresectable, which are located in an inaccessible place in the brain, for surgeons or remove it and surgery may have to destroy or damage nearby healthy brain tissue or cause mortality or severe morbidity such as speech or movement dysfunction [2].

The surgeon determines if a patient's brain tumor is inoperable, so it is advisable to seek a second approach such as streotactic radiosurgery or palliative conventional chemotherapy or radiation therapy [3], but there isn't new radiosurgery method in developing countries or conventional cytotoxic therapy haven't sufficient efficacy. Metronomic chemotherapy[1] is one of inexpensive way can regress inoperable brain tumors such as ependymoma, brainstem glioma, and medulloblastoma and destroy inoperable tumors with different mechanisms (Figure 1).

Anti-angiogenesis effect is common mechanisms of metronomic chemotherapy while prominently decreasing undesirable toxic adverse effects can use for inhibiting unresectable solid tumors ,but main mechanism against inoperable tumors is immuno-surveillance intensification especially T-cells (TREG) inhibition [4].

TREG can inhibit anti-tumor immune response by suppressing the activity of both tumor-specific (CD8+ cytotoxic T lymphocytes and CD4+ T helper cells) and tumor-unspecific effector cells (natural killer [NK] and NK T cells [4].

Increased frequency of TREG cells can correlate with tumor progression and loss of treatment response [5]. Moreover, impairment of TREG activity by either specific blockade or depletion can enhance immune response against tumor-associated antigens [4].

A sample metronomic regimen for meduloblastoma include [6],

- Celecoxib 250 mg/m^2 p. o. b.i.d day 1 to 43.
- Etoposide 50 mg/m^2 p. o. (21 days) plus.
- Cyclophosphamide 2.5 mg/kg/d po day 22 to 43.
- Fenofibrate (90 mg/m^2/d) day 1 to 43.
- Thalidomide (6–12 mg/kg p. o. every day; maximum daily dose 800 mg) day 1 to 43
- Bevacizumab 10 mg/kg weekly day 15 to 29.
- Liposomal cytarabine 25-50 mg intraventricular every 4 week day 29, For median 15.4 months.

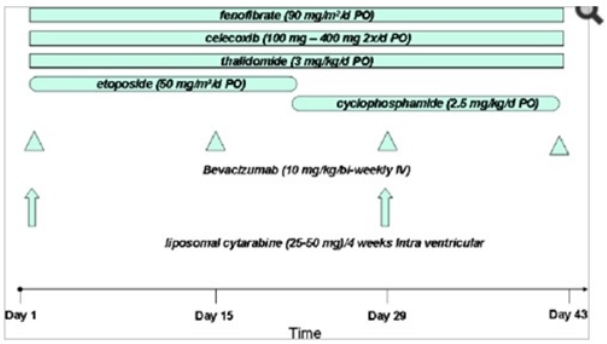

Figure 1: Metronomic multi-target anti-angiogenic for relapsing medulloblastoma.

Although complete responses stay rare, these solutions mainly lead to long-term disease stabilization and significant improvement of the quality of life among children patients with inoperable brain tumors.

Despite clinical success in adults the administration of metronomic treatments in pediatric oncology is still in its early stage as a result of

[1] Metronomic chemotherapy is continuously systemic administration of non-toxic doses, on the proliferating endothelial cells as targets during tumor angiogenesis.

It is type of chemotherapy inhibits tumor progression initially through anti-angiogenic mechanisms while prominently decreasing undesirable toxic adverse effects. Metronomic chemotherapy can induce tumor responses in oncology patients that were resistant to treatment or relapsed after classic chemotherapy. In addition clinical advantage duration obtained with metronomic chemotherapy can be longer than the benefit received with more common approaches. Despite the disparity of efficacy reported for metronomic chemotherapy base on drug combination and tumor type. All of clinical trials proved that this new way, alone or in combination with other treatment options, was well tolerated. High-grade toxic effects doesn't see and are limited a few effects such as grade 1 nausea, vomiting, grade 1 and 2 anemia, neutropenia, leucopoenia and lymphopenia as well as low-grade fatigue.

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the lack of state-of-the-art clinical studies clearly demonstrating efficacy [7], but this approach is an inexpensive option in developing countries.

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