It’s not black or white! Metronomic chemotherapy as a therapeutic option in Metastasis Ewing’s Sarcoma: Case Report

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Abstract

There are currently conventional therapies that have shown a decrease in mortality of pediatric patients diagnosed with cancer, however, some of them suffer from poor prognosis pathologies. In these, the range of available therapies is limited, this is why the use of metronomic chemotherapy as a palliative treatment option has been described. The following is a case report of an adolescent patient with metastatic Ewing’s Sarcoma (ES) that was managed with metronomic chemotherapy (ME) and had a positive impact on functionality, quality of life and opioid requirement.

Keywords: Adolescent; Pediatrics; Ewing’s sarcoma; Metastatic; Metronomic chemotherapy; Palliative treatment; Quality of life

Case Report

A 15-year-old patient, with metastatic ES of the left humerus, skull, ciliary region, left malar and T12 vertebra (Figure 1). At admission, she presented with severe headaches and osteo-muscular pain with a strong opioid-requirement. Due to the extent of the lesions, management with chemotherapy with the POG protocol # 9354 / CCG # 7942 and cranial radiotherapy with curative intention but poor prognosis was initiated. She completed 15 weeks of chemotherapy in 5 months. The pediatric palliative care team began follow-up from the moment of diagnosis.
Through the treatment, she presented with multiple infectious complications and Grade IV hematological toxicity, requiring admission to the intensive care unit. Interim evaluations (Induction and maintenance), revealed a partial response (Figure 2), leading to a clinical discussion of the case, where the pediatric oncology and palliative care team, decided to continue with MC with vincristine, methotrexate, cyclophosphamide and valproic acid (Figure 3) with a palliative intent. A rapid improvement of her functionality (Lansky Scale with Traditional chemotherapy of 50% Vs. 100%), was evidence, as well as a significant pain reduction, decrease and subsequent discontinuation of opioids, absence of toxicity and hospitalizations, and significant impact in her quality of life for 36 months.

Discussion

This case report, in particular, has the purpose of highlighting that MC can impact not only the quality of life, but also the survival of patients with metastatic ES, however, the current evidence is divergent. For example, Robison et al. [11] conducted a multicenter study of 97 pediatric patients with oncological diagnoses as leukemia/lymphoma, bone tumors, neuroblastoma, CNS Tumors, and myelogenous tumors [11], which were managed with different combinations of five chemotherapeutic drugs in metronomic doses including thalidomide, celecoxib, fenofibrate, etoposide and cyclophosphamide, evidencing progression of disease especially in patients with metastatic bone tumor in the 91% of patients within the first 9 weeks after initiation of therapy; concluding, that there was no response in patients with bone tumors. Additionally, recent evidence from a controlled clinical trial[13] in which MC was studied in pediatric patients diagnosed with sarcomas, showed disease progression in a 100% within the placebo group and 94.6% in the MC group over a period of 2.9 months.

Our patient reached a survival of 36 months after the start of the MC. To our knowledge, this is the longest survival reported with the use of this type of chemotherapy. To date, the level of evidence for the use of MC in children is poor, which limits its use. However, there are reports that show that the administration of MC is well tolerated[12] decreases the need for pain medication [12], improves quality of life [13] and may even increase survival [14]. Porkholm et al. reported a case series of 17 patients with central nervous system tumors and solid tumors, treated with a regime of thalidomide, etoposide and celecoxib in a metronomic scheme. They reported an increase in survival in this group of patients [15]. In the same line, A.M. Ali et al., [14] reported 64 patients diagnosed with solid tumors in relapse or with disease progression, in whom a MC regimen consisting of celecoxib, vinblastine, cyclophosphamide and methotrexate was given, and survival of up to 62% was observed during the first-year in treatment [16].

According to these survival projections, the early integration of palliative care in cancer patients becomes even more important. The American Academy of Pediatrics (AAP) has advocated that children with high-risk cancer and other life-threatening conditions have access to “an integrated model of palliative care, from the time of diagnosis and continued throughout the course of the disease, whether the result ends in cure or death” [17]. In this case report we want to highlight the importance of
multidisciplinary management which opens a door to clinical discussion to alternative therapies: neither black nor white, in which the quality of life is prioritized where the goal is “live as long as possible, as well as possible” (shades of gray).

**Conclusion**

In children with advanced cancer disease, it is important to consider the possibility of intermediate therapies with palliative intent. Metronomic chemotherapy represents a therapeutic alternative that can improve functionality, reduce symptoms, prevent rapid disease progression and possibly increase survival.

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**Authors’ contributions**

All authors have read and approved the manuscript, and significantly contributed to this paper: Conception and design, literature review, manuscript writing and correction, final approval of manuscript.

**Ethics approval and consent to participate**

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**Consent for publication**

Written informed consent was obtained from patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**References**


