

Malignant invasive thymoma with chemotherapy alone

Abstract

Thymic tumours the main stay of treatment has always been surgery, followed by radiation and chemotherapy. Herein, is a case of invasive malignant thymoma that was inoperable and refused radiation, but has been treated with an unconventional CMF regimen showing very good response and she continues to remain comfortable.

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Introduction

Malignant thymic invasive tumor has the propensity to invade the pleura, pericardium, and other mediastinal structures. The invasive nature of the tumor renders it inoperable. In such a condition, radiation is the next resort. Ours is case of malignant thymic invasive inoperable tumor who has refused radiation and has been managed in the last 20 months with only chemotherapy. There are several case reports which giving evidence for use of Cisplatin based chemotherapy, Steroids and Octreotide after surgery or radiation or both. However, there are no case reports mentioning only chemotherapy over a prolonged period of time having given partial remission.

Case report

A 56 year old post-menopausal lady was diagnosed to have myasthenia gravis in 2012 September. She was investigated in CMC Vellore and was given pyridostigmine 6 cycles. CT of the thorax showed invasive mass 4.5x4.2cm in the thymus, which was increasing in size. 6 cycles chemotherapy with Cyclophosphamide 700mg every 21 days was given as she was not amenable for surgery. She was advised radiation but she refused radiation. She was given Cyclophosphamide 500mg, Methotrexate 50mg, 5Fluorouracil 500mg every 4 weeks for 13 cycles. January 2014 the repeat CT scan showed reduction in the size of the mass. The CT scan taken in May 2014 showed thymic mass 2.2x3.7cm with calcification, right lower lobe showed sub segmental atelectasis. She has shown partial response to the metronomic chemotherapy and is in good general condition, continuing the same regimen in her native place.

Discussion

Metronomic chemotherapy is known to have antiangiogenic, cytostatic and cytotoxic effect which contributes to its effective anti tumoricidal effect. Strategic selection of drugs used in a continuous metronomic fashion daily, weekly or monthly over prolonged periods lesser than the maximum tolerated dosages but in a low therapeutic dosages is our weapon for the warfare against the disease. The

therapeutically effective anti-angiogenic effects of the metronomic chemotherapy acts like concealed bullets or a poison for the tumor per say though like any other normal chemo regimen it still can have a milder toll on the normal cells. These metronomic-chemotherapy regimens can induce sustained suppression of circulating endothelial progenitor cells, selective inhibition of endothelial cell migration, induction of apoptosis of activated endothelial cells, thereby increasing the levels of the endogenous angiogenesis inhibitor thrombospondin 1, which can eventually suppress neovascularization. Some chemotherapeutic drugs used *in vitro*, are cyclophosphamide and taxanes.¹ These anti-angiogenic mechanisms have been extensively reviewed.²⁻⁵ The classic theory and the more recently discovered putative mechanisms regarding the mechanism of action of metronomic chemotherapy relies on the paradigm initially proposed by Folkman et al.^{6,7} According to this paradigm, by targeting tumor endothelial cells, metronomic chemotherapy is able to destroy drug-naive and drug-resistant cancer cells in an indirect manner by inducing hypoxia and starvation of nutrients. Hypothetically, additional mechanisms of action may be involved.

Thymoma is a common neoplasm in the anterior mediastinum originating from epithelial cells containing admixture of lymphocytes, often presenting with paraneoplastic features such as myasthenia gravis or hypo gamma globinaemia or pure red cell aplasia. Thymoma is best managed by aggressive multimodality therapy with primary modality as surgery followed by radiation and chemotherapy.⁸⁻⁹ There has been trials of preoperative chemo radiation followed by surgery which renders the tumor amenable for surgery.¹⁰ There are not many case reports on the management of invasive malignant thymoma with metronomic chemotherapy in the scenario of inoperability with refusal/denial of radiation. We have several trials using chemotherapeutics in malignant thymic tumors such as follows, cisplatin (50mg/m²);¹¹ single-agent ifosfamide;¹² octreotide (1.5mg/day subcutaneously) with prednisone (0.6mg/kg/day orally for 3 months, 0.2mg/kg/day orally during follow-up);¹³ PAC regimen (cisplatin, doxorubicin, cyclophosphamide);¹⁴ the ADOC regimen (doxorubicin, cisplatin, vincristine, cyclophosphamide);¹⁵ cisplatin and etoposide;¹⁶ etoposide,

ifosfamide, and cisplatin (VIP).¹⁶ The 5-year survival rate for PAC was 32%;¹⁴ ADOC response rate 92%, complete response rate of 43% Cisplatin and Etoposide with a median survival of 4.3 years. VIP 2-year survival is 70%.¹⁶

Here is a case, showing decreasing size of the tumor with a one and a half year period of continuous use of metronomic combination chemotherapy. There is no consensus to decide on the chemotherapeutic treatment regimen for thymoma. Given that the clinical trials are under way to test several combinations of metronomic chemotherapy and anti-angiogenic drugs, we deployed an approved CMF regimen used in Breast cancers and extrapolated its usage on this case of ours in a metronomic manner. The patient has shown significant reduction in the size of the lesion without radiation and surgery over a period of 20 months.

Conclusion

In a developing country, there are often situations when all drugs in a regimen are not available or are expensive to the patients. In these conditions, low dose intravenous maintenance chemotherapy akin to metronomic chemotherapy such as CMF regimen over prolonged periods of time yields very good results in terms of palliation of symptoms, regression of tumours, increasing quality of survival transiting to longer survival. The tailor made regimens with approved drug for metronomic chemotherapy when extrapolated on unusual scenarios such as these, surprisingly yields us significant benefits. This leads to the ground breaking evidence that metronomic chemotherapy is beneficial and can be used in several such scenarios of course with careful monitoring.

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Conflict of interest

The author declares no conflict of interest.

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