



LETTER TO EDITOR

Proposed Experimental Preparation and Administration of Dendritic Cell Vaccine for Treatment of Cancer (Metastatic Castration-Resistant Prostate Cancer)

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Abstract

It is suggested that a cause of inefficacy in dendritic cell vaccine is dendritic cell dysfunction. It is proposed that dendritic cell dysfunction is possibly due to the immune-regulatory function of activated platelets in cancer patients. It is suggested that activated platelets in cancer patient suppress dendritic cell activity against a malignant growth. A low platelet count prior to the removal of dendritic cells would possibly yield less dysfunctional dendritic cells. If a low platelet count persist until a complete platelet turnover occurs possibly then the dendritic cells may be less dysfunctional. Furthermore, possibly a temporary immune paralysis may allow collecting dendritic cells least manipulated by the cancerous growth.

Introduction

Dendritic cells are the most efficient antigen presenting cells. Dendritic Cells play an important function for the induction of innate and adoptive antitumor immune responses. Dendritic cells have an important function to mediating innate immune responses and inducing adoptive immune responses. Platelets have an immune-regulatory function effecting innate immunity cells (NK Cells, Dendritic cell, etc.). Yet the activity of dendritic cells is modified by the immune-regulatory function of activated platelets. Possibly a function of platelet is to protect the integrity of the tissue that activate it even from an immune attack. Platelets are activated by inflammation, either acute inflammation or systemic inflammation. Possibly platelets activated by an acute inflammatory response, signal innate immunity cells (NK Cells, dendritic cells, etc.)

a surveillance mechanism to remove mal functioning cells such as virus infected cells or cancer cells. Possibly platelets that are activated by systemic inflammation induced by the malignancy do signals innate immunity cells (NK cells, dendritic cells, etc.) to abort immune response against the malignancy. Activated Platelets inhibiting NK cells from removing cancer cells is an example [1]. Dendritic cell dysfunction is possibly another example [2]. Platelets promoting angiogenesis and tumor neovascularization is another example. Possibly innate immunity and platelets are contributing to the immunosuppressive microenvironment of the tumor [1]. Therefore, a low count of activated platelets prior the removal of dendritic cells would possibly yield less dysfunctional dendritic cells.

Furthermore, a low count of activated platelets just prior to the administering of dendritic cell vaccines may enhance the effectiveness of dendritic cells vaccine. Possibly the effectiveness of Provenge (Sipuleucel-T) (a dendritic cell vaccine for metastatic castration-resistant prostate cancer) may be enhanced with a prior low platelet count.

Methods

Review and studying the case reports of the spontaneous remission of cancer. Studying the effect of activated platelets in cancer patients on dendritic cells. Reviewing the medical literature for effectiveness of dendritic cell vaccines.



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Results

It appears a low count of activated platelets prior to removal of dendritic cells would possibly yield less dysfunctional dendritic cells due to the immune-suppressive effect of platelets. Possibly if a low platelet count persists until there is a complete turnover of platelets, then drawing dendritic cell from patient may provide with less dysfunctional dendritic cells. Further more, it appears that a low count of activated platelet just prior the administrating the dendritic cell vaccine may have an enhancing effect on the dendritic cell vaccine.

Discussion

In previous papers it was suggested that spontaneous remissions or regression of cancer may occur if a low platelet count is present and accompanied by an acute inflammatory response [3-5]. It seems the same principal may apply to dendritic cell vaccines. It is suggested if dendritic cell vaccine administration is preceded by low count of activated platelet and accompanied with an acute inflammatory response then the dendritic cell vaccine would possibly become more effective. The timing of the acute inflammatory response and the dendritic vaccine administration is of essence. Furthermore, it is important how the dendritic cells are collected to be less dysfunctional.

A basic method to make dendritic cell vaccine is to remove dendritic cells or its precursor from blood. Expose the dendritic cells to autologous tumor antigen *ex vivo* and transfer the dendritic cells back to the patient.

Proposed Experimental Dendritic Cell Vaccine Preparation

The effect of dendritic cell vaccine such as Provenge (Sipuleucel-T), a dendritic cell vaccine for metastatic castration-resistant prostate cancer may be enhanced by how the dendritic cells are collected. A low platelet count prior to collecting dendritic cell. Possibly, a low platelet count maintained until a complete turnover of platelets and then collecting dendritic cells and following with these steps before collecting the dendritic cells possibly may result in less dysfunctional dendritic cells and enhance the effectiveness of dendritic cell vaccine:

- (a) Inducing a temporary immune paralysis by injecting an overload of antigen and afterward collecting dendritic cells. possibly dendritic cells would be less dysfunctional due to prevention of dendritic cell manipulation by the immune system in cancer patients during a temporary immune paralysis**.
- (b) Collecting dendritic cells during an acute inflammatory [6]. Collecting dendritic cells at the time in which innate immunity surveillance (NK cells, Dendritic cells, etc.) becomes activated

- (c) Collecting dendritic cells during concomitant immunity. Excising a small section of the tumor and implanting it at a distant site afterwards collecting the dendritic cells (preferably transplanting at a few different sites)*.

*One may wonder if a low platelet counted followed by the excision of a tumor and transplanting at another site would result in a complete remission of the cancerous growth. Since, platelets seem to disable innate immunity cells (NK Cells, etc.). Concomitant immunity is defined as the inability of the immune system to reject a cancerous growth. Yet, if the same tumor is excised and transplanted at a distant site it would be rejected by the immune system.

**a few acute inflammatory responses within a few hours of each and afterwards collecting dendritic cells during immune paralysis might yield less dysfunctional dendritic cells. Also injecting the host with G-CSF might induce release of stem cells from the bone marrow into the blood that might allow the development of dendritic cells that would be less dysfunctional due to a temporary immune paralysis.

Dendritic Cell Vaccine Administration

The effect of dendritic cell vaccine such as Provenge (Sipuleucel) may be enhanced if prior to its administration: (a) a low platelet count (absence of hyper-coagulation) is present (b) Low dose of a synthetic corticosteroid such as Dexamethasone or Prednisone administered [7] (c) combined with an acute inflammatory response such as one of the following:

- 1) G-CSF administration preferably subcutaneous administration timing with Provenge is such to induce optimum innate immunity response [5] (G-CSF may lower platelet count, therefore a prior low platelet count might become excessive).
- 2) Tissue inflammation [8], preferably tissue close to a primary tumor of an aggressively growing tumor. Timing with Provenge is such to induce optimum immune reaction.
- 3) Injection of non-live vaccines (Tetanus, Diphtheria, Singles, Pneumonia, etc.) timing with Provenge is such to induce optimum acute inflammatory response [9].
- 4) An allergic reaction by an allergen timing with Provenge is such to induce an optimum acute inflammatory response.
- 5) Injection of Plasma rich platelet (high leucocyte) timing with Provenge is such to induce optimum acute inflammatory response.

Dendritic cell vaccine has been used for the treatment of prostate cancer. FDA has approved Provenge (Sipuleucel) a dendritic cell vaccine for the treatment of castration-resistant prostate cancer. A

favorable time to use Provenge might be in the event of “anti-androgen withdrawal syndrome”. A drop of PSA after anti-androgen withdrawal is considered as the “anti-androgen withdrawal syndrome”. A doctor may monitor his patient closely after anti-androgen withdrawal. If anti-androgen withdrawal syndrome noticed immediately place the patient on Provenge (Sipuleucel). If accompanied by a low dose of a synthetic corticosteroid such as prednisone or cortisone possibly the chances of a prolonged remission will increase. If a cancer patient has become resistant to anti-androgen therapy it might not be a bad idea to start dendritic cell vaccine just prior to withdrawal of anti-androgen therapy accompanied with a low dose of synthetic corticosteroid. If a low platelet count is present prior to the withdrawal of anti-androgen therapy possibility the effectiveness of Provenge will increase.

Caution

A hypothesis has been suggested without any experimental proof for its correctness.

Medical supervision required for Experimental Treatment.

Platelet count may drop too low and cause spontaneous bleeding.

Combination of low platelet count and injection of a non-live vaccine may result in bleeding.

Close monitoring of patient needed.

Disclaimer

Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because you have read this study.

This is not intended to be a substitute for medical advise, diagnosis, or treatment in regards to any patient.

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