Harnessing Immune Switch Responses in Relapse of Ovarian Cancer: All Signals Needed

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Introduction

The immune system plays an important role in controlling and elimination of cancer. Persistent infection and/or inflammation leads to gradual accumulation of tolerant apoptotic or immunosenescent cells within host body. Temply, how to trigger antigen-presenting cells generate and/or amplify host immunosurveillance after optimal debulking operation to be a central role. Advanced invasive ovarian cancer after conventional therapy, they still faced 60-70% disease relapse. Once relapse, they suffered from detrimental outcome following first-line treatment. Thus, clinician has to do early imaging and/or tumor markers' screening as well as possible and early intervention of integrated therapy for relapse of ovarian cancer.

Clinician has to educate relapse of cancer patient and/or families to tolerate and understand common cold-like fever to elicit "signal 0, to mimic anger signal" following immunomodulatory therapy [1]. OK-432 one vial administration of subcutaneous skin to trigger dendritic cells' (DC) activation and present innate Toll-like receptor to capture cancer-associated antigen to solicit Toll-like receptor (TLR) 4-MD2 signal pathway. Ok-432 as adjuvant agent trigger DCs reside in tissue or peritoneal macrophages to capture antigen to form an efficient vaccine to link innate cells and adaptive immune cells to elicit host immunosurveillance [2].

Ok-432 is a useful adjuvant in DC-based anticancer immunotherapy. Administration of subcutaneous OK-432 injection to activate antigen presenting cells including macrophages and/or dendritic cells to secret multiple cytokines to generate efficient anti-cancer response. The effects of OK-432 on DCs recognize cancer-associated antigens (vaccines) to mimic signal 1 and secrete cytokines (e.g. IL-12, IFN-alpha and interferon-gamma production) directly through Toll-like receptor, and adaptive cells' receptor and stimulation of costimulatory molecules (e.g. CD40, CD80, CD83, CD86, HLA-DR, etc.) to mimic signal 2 to generate a vaccine [2]. IL-2 is a cytokine for T lymphocytes' growth (e.g. CD40, CD80, CD83, CD86, HLA-DR, etc.) to mimic signal 3 and secrete cytokines (e.g. IL-12, IL-18, IFN-alpha and interferon-gamma production) directly through Toll-like receptor, and adaptive cells' receptor and stimulation of costimulatory molecules (e.g. CD40, CD80, CD83, CD86, HLA-DR, etc.) to mimic signal 4 to generate a vaccine [2]. IL-2 is a cytokine for T lymphocytes' growth to mimic signal 3. IL-2 treatment triggers chemokine receptor CXCR4 expression on Treg cells, enables Treg cells migration toward chemokine CXCL12 in tumor microenvironment, and may enforce Treg cell tumor accumulation [3]. Type I interferons (alpha/beta) keep CXCR4 expression on Treg cells, enable Treg cells migration toward chemokine CXCL12 in tumor microenvironment, and may enforce Treg cell tumor accumulation [3]. Type I interferons (alpha/beta) keep CXCR4 expression on Treg cells, enable Treg cells migration toward chemokine CXCL12 in tumor microenvironment, and may enforce Treg cell tumor accumulation [3].

A single administration of cyclophosphamide was shown to deplete CD4+CD25+ T cells in tumor-bearing animals, delay tumor growth, and cure rats bearing established tumors when followed by an immunotherapy which has no curative effect when administered alone. Both host immunologic and intraperitoneal micrometastatic factors have been examined with immunomodulatory therapy (IMT) or bevacizumab (avastin). Subcutaneous administered IMT switch type 2 immune cells to type 1 immunosurveillance cells. Intraperitoneal avastin administered to neutralize aberrant VEGF expression to enhance conventional chemotherapy and/radiotherapy for relapse of ovarian cancer [4].

Case Demonstration

A case birth on August 1968 female, Gravida 2 Paravida 2, suffered from general abdominal pain and tenderness in 2009. A 44-year-old female diagnosed with advanced ovarian cancer stage 4 with liver metastasis was treated with suboptimal debulking surgery and received conventional chemotheraphy. Within one year, on May 2010, she had abnormal CA-125 increased and PET-CT showed peritoneal carcinomatosis. She again received hyperthermia and intraperitoneal chemotheraphy during operation. Due to CA-125 still high level, she had bowel obstruction on December 2011. She requested to do immunomodulatory therapy to want to achieve "proof-of-concept" to control her peritoneal carcinomatosis scerions on January 2012. The priming immunomodulatory agents include picibanil (OK-432) at day1 and adleleukin (A: interleukin-2) at day 2. She received celexocib twice tablet daily. 2 days later, she agreed to do more alternatively immunomodulatory therapy as booster immunization. No fever onset, 24 to 48 hours later, 1 administered low dose chemotherapy one vial such as paclitaxol or lipodoxil to create host immunosurveillance and hold cancer cell progression or avoid host immunocompromised status. She had progression free interval for over 12 months and/or better life span with normalization tumor marker to make her better spirit after immunomodulatory therapy (Figures 1 and 2).

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Figure 2: We hold and persistent suppress patient’s to worry about stabilization of tumor marker CA-125.

References


