Up-to-date immunochemo thrapy of lymphomas

Mona Mohammad El Balshi

The aim of this essay is to review the up-to-date literature about:• The development of immunochemotherapy.• The mechanism of action of immunochemotherapy in lymphomas.• The role of immunochemotherapy in the management of lymphomas.• Comparing the role ofCytotoxic chemotherapy targets dividingimmunochemotherapy with that of traditional chemotherapy of lymphomas.cells, including tumor cells and lymphocytes. Thus chemotherapy could be regarded as antagonistic to immunotherapy. However, recent finding suggest that chemotherapy can improve the effects of immunotherapy via a series of mechanisms (480). Cell death induced by chemotherapeutic drugs is often accompanied by tissue necrosis and the release of a number of danger signals that -lead to the activation of immune cells and facilitate tumor antigen cross presentation and cross priming both in vitro and in vivo (481). Chemotherapy is associated with lymphodepletion that can be beneficial because it leads to the elimination of regulatory T cells as well as of poorly functional anti-tumor T cells, and to the creation of ‘space’ for the development of new more effective anti-tumor specific T cells that undergo homeostatic proliferation. In this context the combination of chemotherapy before immunotherapy can have the multiple effect of eliminating T regs, facilitating tumor antigen cross-presentation and engraftment of new more effective lymphocytes. Immunomodulatory effects have been described for several cytooxic agents: cyclophosphamide, gemcitabine, adriamycin, taxanes and 5- fluorouracil. The combination best studied is that of immunotherapy with Cyclophosphamide. Cyclophosphamide is a DNA alkylating agent overly used to treat haematological and solid malignancies. The effect of cyclophosphaide is best appreciated at low dose actin as an immunostimulator via both the elimination and inactivation of T regs (482). The Combination of cyclophosphamide and immunotherapy has been tested in several tumor settings in humans. Low dose radiation has been described to exert an immunomodulatory activity on a mouse adenocarcinoma cell line by inducing the upregulation of MHC class I expression and expanding the intracellular peptide pool. For this reason, the treatment of cutaneous tumor lesions with local radiotherapy was proven to be a valuable supplement to enhance the efficacy of adoptive tumor immunotherapy. In fact, the combination of adoptively transferred tumor-specific transgenic T cells plus local irradiation with 10 Gy led to complete eradication of established tumors in mice bearing transplantable colon adenocarcinoma and fibrosarcoma subcutaneously. Radiation has also been shown to facilitate tumor antigen cross presentation in prostate cancer patients (483). Altogether these observations suggest that

radiotherapy coupled to immunotherapy can lead to superior immunotherapy. Besides the described potentiating effects of chemo- or radiotherapy over immunotherapy, the advantage of using the combination is that the patients will still receive standard therapy while being treated with immunotherapy, facilitating the approval of protocols for ethical reasons. (483)