Peripheral leukocyte response to oncological radiotherapy: Expression of Heat Shock Proteins

M. C. GUIASOLA 1, F. CALVO 2, P. MARCOS 2, I. SIMÓN 1, F. J. VILLANUEVA 1, E. ANDRÉS 2, A. SUÁREZ 1 & P. GARCÍA-BARRENO 1

1 Cellular Biology Laboratory, Experimental Medical and Surgery Unit, and 2 Oncology Department Hospital General Universitario Gregorio Marañón, Madrid, Spain

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Abstract

Purpose: To study Heat Shock Proteins (HSP) expression in patients subjected to radiotherapy and their potential use as biomarkers for radiation tolerance. An evaluation is also made of whether irradiated volume is critical to the outcome of normal tissue injury using polymorphonuclear neutrophils as biosensors, and whether HSP antibodies (Ab) may be involved in post-radiotherapy disease.

Material and methods: Twelve patients receiving the same total dose of radiotherapy, but in three different volumes, and four healthy volunteers used as controls were analysed. hsp 27 and 70i mRNA were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and Southern-blot, HSP by flow cytometry, and HSP-Ab by Enzyme-linked Immunoabsorbent Assay (ELISA). The clinical protocol included radiation related toxicity based on clinical and analytical scales.

Results: Radiotherapy caused hsp downregulation, maximum in patients with the largest irradiated volumes, and a decrease in intracellular HSP content. Patients with greatest intraleukocyte HSP levels before treatment suffered more severe radiation morbidity. Patients with endocrine neoplasms presented the highest HSP-Ab titers.

Conclusions: Radiotherapy downregulates hsp 27 and 70i, which would enhance radiosensitivity. HSP content prior to treatment is suggested as a prognostic biomarker for radiation tolerance, with circulating leukocytes as biosensors. HSP-Ab may be biomarkers of tumor disease, but do not seem to be involved in the morbidity of acute post-radiotherapy disease, which is closely related to the volumes irradiated.

Keywords: Stress proteins, radiotherapy, leukocytes, immunology, gene expression, cell biology, flow cytometry

Introduction

It is widely known that among a group of patients undergoing the same radiation treatment, some will show more severe normal tissue reactions than others. The causes underlying these differences include dosimetry, treatment volume, tissue, physiology, and genetics. If methods for predicting susceptibility to radiation damage could be developed, two courses of action would be opened: The reduction of radiation volume in susceptible patients, or an increase in volume in non-susceptible patients. A third option would be the activation of protocols to manipulate factors protecting from radiation effect (Sanchez-Nieto et al. 2001). Evidence of the feasibility of predicting normal tissue damage originally came from skin biopsies from untreated areas (Haikonen et al. 2003), but blood leukocytes are more accessible for evaluation purposes and have been shown to be effective biosensors in multiple diseases (Fehrenbach et al. 2000, Hashiguchi et al. 2001).

Stress responses affect the physiological and pathological characteristics of various organisms. The main event associated with stress responses is the synthesis of stress proteins (particularly Heat Shock Proteins [HSP]). Organ HSP expression to a sufficient level confers resistance to damage (Morimoto & Santoro 1998), which may provide a basis for therapeutic and preventive treatments of certain diseases. Since HSP are ubiquitous proteins, they might be potential biomarkers for multiple diseases (Welch 2001). HSP and their derived peptides have particular...