CHAPTER 14

SOLAR ULTRAVIOLET RADIATION, VITAMIN D AND SKIN CANCER SURVEILLANCE IN ORGAN TRANSPLANT RECIPIENTS (OTRS)

An Update

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Abstract: During the last decades, the annual numbers of performed solid organ transplants have continuously increased world-wide. Solid organ transplant recipients (OTR) have a greater risk to develop malignancies, with skin cancer representing the most common neoplasia. Additionally, OTRs in general develop a more aggressive form of malignancies. In consequence, dermatologic surveillance is of high importance for OTRs and these patients represent an increasing and significant challenge to clinicians including dermatologists. In OTRs, patient and organ survival have increased considerably and continuously over the past two decades as a result of better immunosuppressive regimens and better posttransplant care. Great progress has been made in our understanding that individual immunosuppressive regiments differ in their effect on skin cancer risk in OTRs, and that effects of individual immunosuppressive regimens on skin cancer risk depend on various other factors including viral infections. Since sunlight is the major source of vitamin D for most humans, OTRs, who have to protect themselves consequently against solar or artificial UV radiation, are at high risk of developing vitamin D deficiency. Vitamin D deficiency is not only associated with increased risk for metabolic bone disease, but with other severe health problems including various types of malignancies. As a consequence, screening for and treatment of vitamin D deficiency is warranted in OTRs. In this review, we give an update on our present understanding of skin cancer surveillance in OTRs.


INTRODUCTION

During the last decades, the annual numbers of performed solid organ transplants has continuously increased world-wide. In line with this observation, it has been reported by the United Network for Organ Sharing, that in the United States of America (US) alone, over 25,000 solid organ transplantations were performed in 2003 (based on OPTN data as of January 1, 2004). It is well accepted, that solid organ transplant recipients (OTR) have an increased risk to develop malignancies, with skin cancer representing the most common neoplasia. Additionally, OTR in general develop a more aggressive form of malignancies. In consequence, dermatologic surveillance is of high importance for OTR, who represent an increasing and significant challenge to clinicians including dermatologists. In OTRs, patient and organ survival have increased considerably and continuously over the past two decades as a result of better immunosuppressive regimens and better posttransplant care. However, it now has become evident that the more effective immunosuppression regimens have as an unintended consequence resulted in more frequent and aggressive skin cancers. It has been convincingly demonstrated that the incidence of skin cancer increases with survival time after transplantation. The biological behavior of malignant skin tumors demonstrates in OTR a much more aggressive profile when compared with the non-immunosuppressed population, leading to considerable cutaneous morbidity, mortality and decrease in quality of life.

THE FIRST CHALLENGE: INCREASED INCIDENCE AND PREVALENCE OF NONMELANOMA SKIN CANCER (NMSC) IN SOLID ORGAN TRANSPLANT RECIPIENTS

Nonmelanoma skin cancer (NMSC), most importantly basal cell carcinomas (BCC) and cutaneous squamous cell carcinomas (SCC) represents the single most commonly diagnosed malignancy in the Caucasian population. In the US alone, an estimated 1 million new cases are reported each year. Cutaneous SCCs are in general easily managed in immunocompetent individuals where they rarely grow aggressively or metastasize. However, when SCCs develop in patients who have been immunosuppressed over long time periods (e.g., in OTRs), they grow aggressively and are a difficult management problem with substantial morbidity and mortality. It has now been convincingly demonstrated that NMSC accounts for appr. 90% of all skin cancers in transplant recipients. While SCC has been reported to represent the most common skin cancer in transplant recipients occurring up to 250 times as frequently as in the general population, the incidence of BCC is increased by a factor of appr. Ten in solid OTRs. Following transplantation, the usual BCC/SCC ratio in the general population (4:1 in higher latitude, respectively 2.5:1 in lower latitude) reverses in favor of SCC up to rates > 3:1. These differences are most likely markedly caused by differences in genetic backgrounds, skin types and sun exposure habits at different latitudes.

In recent years, it has been convincingly shown that the incidence of NMSC increases continuously with the duration of the time period after transplantation and with the level of immunosuppression. Additionally, recent data indicate that solar and artificial ultraviolet (UV)-exposure both before and after organ transplantation increase the risk to develop skin cancer and that the incidence of NMSC varies with the type and dose of immunosuppressive medication used. As an example, it has been reported that in Australia,