Secondary Neoplasias following Chemotherapy, Radiotherapy, and Immunosuppression
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Reports of secondary neoplasia developing after successful curative chemotherapeutic or radiotherapy for malignancies are increasing. Also of growing concern is the diagnostic and therapeutic problem of tumorigenesis during posttransplantation immunosuppressive therapy. With chapters contributed by internationally renowned researchers, this book discusses several aspects of this issue.

The first part covers the various causes of primary and secondary tumorigenesis and of neoplasia occurring during posttransplantation immunosuppressive therapy. As survival times lengthen and overall remission rates increase for patients with Hodgkin’s disease, germ-cell tumors, non-Hodgkin’s lymphomas or leukemia, the potential risk of developing therapy-associated secondary malignancy is becoming a focus of attention. What makes this problem even more relevant are the many breast and colon carcinoma patients who receive adjuvant chemotherapy after complete resection of the primary tumor or even of metastases. In addition, an increasing number of patients with chemosensitive disease are receiving high-dose chemotherapy with autologous peripheral-blood stem-cell transplantation.

Post chemotherapy, the most common secondary neoplasm is secondary acute myeloid leukemia, which develops primarily after treatment with alkylating agents or topoisomerase inhibitors. While secondary leukemia after alkylating-agent therapy often commences with a preleukemic phase of myelodysplasia, secondary leukemia associated with epipodophyllotoxin is acute, and lacks this preceding myelodysplasia. The correlating chapters in this book discuss in depth the risk of the individual cytostatic agents for inducing secondary malignoma, and include the aspects of cumulative dose dependency and chronology of administration.

Other chapters discuss the role of immunosurveillance and the immune system’s recognition of tumors. In this area, our knowledge is constantly growing, in
particular with respect to the molecular processes responsible for the changes on tumor cells and immune cells, the structure and function of a wide variety of surface receptors and ligands on these cells, lymphocytic signal transduction pathways, the characterization of murine tumor-specific transplantation antigens, and human tumor-associated antigens. Although far from complete, our understanding of cellular immune response to tumors has improved considerably, as has our understanding of how tumor cells escape detection by the immune system.

As more and more tumors develop during posttransplantation immunosuppressive therapy, today’s findings on the underlying processes will lead to innovative changes in existing therapeutic concepts. Already, we must increasingly deal with aspects such as the antigenic characteristics of transformed cells, host-tumor interaction, molecular mechanisms of cell-dependent cytotoxicity, identification of components that generate and control effective immune response, induction of tolerance or of T-cell anergy, and immunologic effects of the host on the neoplastic growth of tumor cells. One therapeutic aspect is the modulation of the immune system or of tumor cells such that the latter can be more easily recognized and eliminated by immunoeffectors. In addition, this book covers the role and significance of herpesviruses in these areas.

The last part of this book discusses the prevention of secondary tumors and tumors occurring during immunosuppressive therapy. Here, the major substances for cytoprotection during chemo- and/or radiotherapy are presented. Also described are new vaccine strategies for treating varicella- and herpesvirus-associated tumors. These vaccines can be applied not only for treatment of infections, but are beginning to play an important role in tumor prevention as well. Of special interest is the chapter dealing with immunomodulatory therapy of posttransplantation lymphoproliferative disorders.

The authors repeatedly stress that early detection is a prerequisite for successful treatment of secondary neoplasms and neoplasms occurring during immunosuppression. Therefore, patients who are successfully treated for malignancy in particular require long-term follow-up including checks for therapy-associated late sequelae. However, this applies also to patients who, after organ transplantation, receive immunosuppressive therapy.

In closing, we can again only reiterate that our international group of authors underscores the importance of global collaboration if we are to find diagnostic and therapeutic solutions to these problems.

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