 ISBN: 978-81-941253-2-7

CANCER IMMUNOTHERAPY

Bijaylaxmi Parida and Pankaj Meher
Department of Zoology, School of Applied Sciences, Centurion University of Technology and Mangement, Odisha

ABSTRACT
Compared with previous standards of care (including chemotherapy, radiotherapy, and surgery), cancer immunotherapy has brought significant improvements for patients in terms of survival and quality of life. Immunotherapy has now firmly established itself as a novel pillar of cancer care, from the metastatic stage to the adjuvant and neoadjuvant settings in numerous cancer types. In this review article, we highlight how the history of cancer immunotherapy paved the way for discoveries that are now part of the standard of care. We also highlight the current pitfalls and limitations of cancer checkpoint immunotherapy and how novel research in the fields of personalized cancer vaccines, autoimmunity, the microbiome, the tumour microenvironment, and metabolomics is aiming to solve those challenges.

Keywords: Immune checkpoint inhibitors, personalized cancer vaccines, immune-related adverse events, microbiome studies, metabolomics

INTRODUCTION

The field of immuno-oncology has been transformational in the care of cancer patients. William B. Coley, now widely accepted as the father of immunotherapy, first attempted to harness the power of the immune system for treating cancer in the late 19th century. As an orthopedic surgeon who operated on patients with bone sarcomas, he noticed that some patients with significant postoperative wound infections—a common occurrence when aseptic technique had not yet been optimized—would undergo spontaneous regression of their unresected tumours. Beginning in 1891, Coley injected more than a thousand patients with mixtures of live and inactivated bacteria such as *Streptococcus pyogenes* and *Serratia marcescens* with the hope of inducing sepsis and strong immune and antitumour responses. His cocktail of bacteria became widely known as "Coley's toxin" and represents the first documented active cancer immunotherapy intervention[1]. Coley achieved durable complete remissions in several types of malignancies, including sarcoma, lymphoma, and testicular carcinoma. However, the lack of a known mechanism of action for Coley's toxin and the risks of deliberately infecting cancer patients with pathogenic bacteria caused oncologists to adopt surgery and radiotherapy as alternative standard treatments early in the 20th century[2].

It would take more than half a century before a better understanding of the key mediators of sepsis would shed some light on the mechanisms of action of Coley's toxin. Those mediators constitute a cytokine family including interleukins, interferons, and chemokines[3]. Once again, the race was on to apply those novel discoveries to cancer therapy[4]. Physicians and researchers achieved modest success with this novel approach, occasionally inducing clinical remissions with high-dose interleukin 2 (IL-2) in metastatic renal cell carcinoma[5] and debatable responses with interferon in stages III and IV melanoma[6]. Those modest successes were often counterbalanced with significant adverse events. Although novel methods of delivery such as pegylation would abate some of the toxicities, the sporadic and unpredictable immune responses seen with those therapies meant that only a small, carefully selected subgroup of cancer patients would benefit.

The next revolutionary wave in cancer immunotherapy came with the better understanding of the process of immune surveillance, by which innate immune cells eliminate cancer cells. The recent discovery of T cell immune checkpoints, such as CTLA-4 and PD-1, propelled the field of immuno-oncology into its current era and saw the awarding of the 2018 Nobel prize in Physiology or Medicine to Drs. Allison and Honjo. Those hardwired signals have the crucial task of maintaining a fine balance between immune surveillance against foreign pathogens or abnormal cells and autoimmunity. Blocking those T cell surface receptors results in enhanced autoimmunity that induces an immune response against tumours, but can also increase the chance of autoimmune reactions.

In this review article, we highlight the current standards of care in cancer immunotherapy, with a strong focus on immune checkpoint inhibitors (ICIs), their limitations and pitfalls, and promising novel approaches.