The interface of cancer immunotherapy and immunopathology: Adverse events and tissue reactions.

Sarah Y. Chen*

Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX, USA.

Introduction

Cancer immunotherapy has revolutionized oncology by harnessing the power of the immune system to combat tumors. Therapies such as immune checkpoint inhibitors (ICIs), chimeric antigen receptor (CAR) T-cell therapy, and cancer vaccines have significantly improved survival in various malignancies. However, the activation of the immune system, while beneficial for tumor control, can lead to unintended tissue damage and immune-related adverse events (irAEs), highlighting the critical intersection of cancer immunotherapy and immunopathology.

The most widely used immunotherapeutic agents—immune checkpoint inhibitors—target regulatory molecules such as cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), programmed cell death protein 1 (PD-1), and its ligand PD-L1. By blocking these inhibitory checkpoints, ICIs unleash T cells to mount robust antitumor responses. However, this immune activation can become dysregulated, leading to T-cell–mediated inflammation against self-tissues, akin to autoimmune disease. This phenomenon underlies many irAEs observed in clinical practice.

Immune-related adverse events can affect virtually any organ system. The skin, gastrointestinal tract, liver, lungs, and endocrine glands are the most commonly involved. Dermatologic reactions such as rash and pruritus often occur early and are generally mild. In contrast, colitis, pneumonitis, hepatitis, and hypophysitis can be severe or even life-threatening if not promptly diagnosed and treated. Histopathologically, these irAEs often resemble classic autoimmune conditions—for example, lymphocytic infiltration and crypt abscesses in colitis, or granulomatous inflammation in lung tissue during pneumonitis [1-5].

The immunopathological basis of irAEs involves excessive T-cell activation, loss of peripheral tolerance, and expansion of autoreactive T or B cell clones. For instance, PD-1 normally suppresses immune responses in peripheral tissues; its blockade may allow T cells to attack nonmalignant cells expressing shared antigens. Additionally, some tumors express antigens similar to those found in normal tissues, leading to cross-reactivity and tissue damage. The presence of pre-existing autoantibodies or underlying subclinical autoimmunity may further predispose patients to irAEs.

CAR T-cell therapy, which involves genetically engineered T cells targeting tumor antigens, introduces a distinct set of immunopathological challenges. One of the most feared complications is cytokine release syndrome (CRS), marked by high levels of pro-inflammatory cytokines such as IL-6, IL-1, and IFN-γ. CRS can manifest with fever, hypotension, and multi-organ dysfunction, requiring immunosuppressive management. Another significant toxicity is immune effector cell-associated neurotoxicity syndrome (ICANS), which involves neuroinflammation and can lead to encephalopathy, seizures, or coma [6-10].

Managing irAEs requires a delicate balance between suppressing pathological inflammation and maintaining antitumor immunity. Corticosteroids are the first-line treatment for most moderate to severe irAEs, and other immunosuppressants like infliximab or mycophenolate may be used for refractory cases. Importantly, early recognition and intervention are critical to prevent long-term damage or fatal outcomes.

Conclusion

In conclusion, while cancer immunotherapy represents a paradigm shift in oncology, its interface with immunopathology necessitates careful monitoring and understanding of immune-mediated tissue reactions. A multidisciplinary approach involving oncologists, immunologists, and pathologists is essential for optimizing patient outcomes and managing the complex landscape of immunotherapy-induced adverse events.

References

1. Jahn SW, Plass M, Moinfar F. Digital pathology: advantages, limitations and emerging perspectives. J Clin Med. 2020;9(11):3697. 2022.
2. Notarte KI, Ver AT, Velasco JV et al . Effects of age, sex, serostatus, and underlying comorbidities on humoral response post-SARS-CoV-2 Pfizer-BioNTech mRNA vaccination: a systematic review. Crit Rev Clin Lab Sci. 2022:1-8. 2021;12(1):1-4.
3. Chagla Z The BNT162b2 (BioNTech/Pfizer) vaccine had 95% efficacy against COVID-19≥ 7 days after the 2nd dose. Annals Internal Med. 2021;174(2):JC15

***Correspondence to:** Sarah Y. Chen, Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX, USA. E-mail: sychen@utswmed.edu

***Received:** 14-Feb-2025, Manuscript No. AACPLM- 25-164072; **Editor assigned:** 15-Feb-2025, Pre QC No. AACPLM- 25-164072 (PQ); **Reviewed:** 17-Feb-2025, QC No. AACPLM-25-164072; **Revised:** 18-Feb-2025, Manuscript No. AACPLM- 25-164072 (R); **Published:** 23-Feb-2025, DOI: 10.35841/ aacplm-7.1.252*

***Citation:** Chen SY. The interface of cancer immunotherapy and immunopathology: Adverse events and tissue reactions. J Clin Path Lab Med.2025;(7)1:252*

4. Niazi MK, Parwani AV, Gurcan MN. Digital pathology and artificial intelligence. Lancet Oncol. 2019;20(5):e253-61.

5. Purushothaman A, Uyama T, Kobayashi F, et al. Heparanase-enhanced shedding of syndecan-1 by myeloma cells promotes endothelial invasion and angiogenesis. Am J Hematol. 2010;115(12):2449-57.

6. Zikos TA, Clarke JO. Non-acid reflux: When it matters and approach to management. Curr Gastroenterol Rep. 2020;22(9):1-0.

7. Horton A, Gyawali CP, Patel A. . Non-acid Reflux: What to Do When You Don't Feel the Burn. J Dig Dis. 2021;66(4):929-31.

8. Mitchell DR, Derakhshan MH, Robertson EV, et al. The role of the acid pocket in gastroesophageal reflux disease. J Clin Gastroenterol. 2016;50(2):111-9.

9. Marjot T, Ray DW, Williams FR, et al. Sleep and liver disease: a bidirectional relationship. Lancet Gastroenterol Hepatol. 2021;6(10):850-63.

10. Gautheron J, Gores GJ, Rodrigues CM. Lytic cell death in metabolic liver disease. J Hepatol. 2020;73(2):394-408.

Citation: *Chen SY. The interface of cancer immunotherapy and immunopathology: Adverse events and tissue reactions. J Clin Path Lab Med.2025;(7)1:252*