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Opinion Article

Adverse Events in Cancer Immunotherapy: Management and Prevention Strategies

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DESCRIPTION

Cancer immunotherapy has revolutionized cancer treatment by enhancing the body's immune system to target and destroy cancer cells. Treatments such as immune checkpoint inhibitors, CAR-T cell therapy and cancer vaccines have shown remarkable efficacy in various malignancies. However, these therapies are not without risks, as they can lead to Adverse Events (AEs) that range from mild to life-threatening. Effective management and prevention strategies are essential to maximize the therapeutic benefits while minimizing harm to patients.

The adverse events in cancer immunotherapy are primarily immune-related, given that these treatments modulate the immune system. Common adverse events includes immune-related Adverse Events (irAEs) are a result of the immune system attacking normal tissues and organs. They can affect any organ system, but common irAEs include dermatitis, colitis, hepatitis, pneumonitis, and endocrinopathies such as thyroiditis and hypophysitis.

Cytokine Release Syndrome (CRS) is frequently associated with CAR-T (Chimeric Antigen Receptor T) cell therapy; CRS occurs when activated immune cells release large amounts of cytokines into the bloodstream, leading to systemic inflammation. Symptoms can range from mild flu-like symptoms to severe life-threatening conditions, including multi-organ failure. Neurotoxicity is also associated with CAR-T cell therapy, neurotoxicity can manifest as headaches, confusion, seizures, or even coma. This condition is often referred to as Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS). These occur during or shortly after the administration of immunotherapies, particularly monoclonal antibodies. Symptoms can include fever, chills, rash, and hypotension.

The mechanisms driving these adverse events are closely related to the therapeutic action of immunotherapies. Immune Checkpoint Inhibitors are drugs that block inhibitory pathways which normally keep immune responses in check, such as CTLA-4 and PD-1/PD-L1. While this enhances anti-tumor immunity, it can also lead to autoimmunity and inflammation in normal tissues. CAR-T Cell Therapy involves engineering T cells to express Chimeric Antigen Receptors (CARs) that recognize cancer-specific antigens. The activation and expansion of these CAR-T cells can lead to excessive cytokine production, causing CRS and neurotoxicity. Cancer vaccines and other immunotherapies treatments stimulate the immune system to recognize and attack cancer cells, but can also result in off-target effects where normal tissues are attacked.

Effective management of adverse events in cancer immunotherapy involves early detection, prompt intervention, and tailored treatment strategies. Regular monitoring of patients receiving immunotherapy is essential for early detection of adverse events. Corticosteroids are the first-line treatment to reduce inflammation. In refractory cases, additional immunosuppressants like infliximab or mycophenolate mofetil may be used. Management of CRS involves supportive care, including antipyretics for fever and fluids for hypotension. In severe cases, tocilizumab, an IL-6 receptor antagonist, and corticosteroids are used. Neurotoxicity management may include corticosteroids and supportive neurological care. In cases of severe or life-threatening adverse events, temporarily interrupting or permanently discontinuing immunotherapy may be necessary to prevent further harm.

Preventing adverse events in cancer immunotherapy involves proactive measures to minimize risks: Identifying patients at higher risk for adverse events based on their medical history, comorbidities, and baseline immune function can help tailor treatment plans and mitigate risks. For high-risk patients, prophylactic measures such as premedication with corticosteroids or antihistamines before immunotherapy infusion can reduce the risk of infusion reactions and other early-onset adverse events. Educating patients about the potential adverse events, signs and symptoms to watch for, and when to seek medical attention is essential for early intervention.

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