

Side effects of immunotherapy

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Immunotherapy offers new hope for cancer patients. Immune checkpoint inhibitors (ICIs) are a new class of immune modulating monoclonal antibodies, used in the treatment of a variety of cancers. These drugs target molecules expressed on either the surface of T lymphocytes (CTLA-4, PD-1) or on the tumour cells themselves (PD-L1), and allow an anti-tumour immune response to be generated, potentially giving patients durable tumour control or complete remission.

Part of the rapid drug development involves combination immunotherapies, which also increases the risk of toxicities. Toxicities are mainly due to the dysregulation of the immune system caused by these drugs and the off-target effect on organ systems. Toxicities are novel and across multiple disciplines, and the key to patient safety is recognition and prompt discussion with the treating specialist to allow early appropriate intervention.

A challenge is to raise awareness about the side effect profile of immunotherapy. Although, toxicities can be more favourable than with chemotherapy, some adverse events if left untreated can be fatal. Moreover, immune-related adverse effects (irAE) can sometimes appear late into treatment or even after treatment completion.

Skin toxicity is most common

Rash and/or pruritus can occur in up to 50% of patients and is typically described as reticular, erythematous and/or maculopapular. Other less common skin manifestations

include vitiligo, alopecia and Stevens Johnson Syndrome/ Toxic Epidermal Necrolysis.

Gastrointestinal

Diarrhoea can also be associated with colitis, for which symptoms include abdominal pain, mucous or blood in the stool. Rare complications of colitis include bowel obstruction and perforation. Infectious causes of diarrhoea should be considered, however, physicians should have a low threshold to suspect immune related adverse effects.

Hepatotoxicity

Immune-related hepatitis is largely asymptomatic and noted on routine blood tests. Mild elevations in liver enzymes can be treated expectantly but more severe derangements need prompt therapy.

Endocrinopathies

Hypopituitarism caused by autoimmune hypophysitis is a common endocrine irAE. Symptoms include headache, nausea, vertigo, behavioural changes and visual disturbances.

Other immune related endocrinopathies include hyperthyroidism, hypothyroidism, hypogonadism and type I diabetes.

Tests include serum hormone levels to assess pituitary function, with electrolytes and glucose levels. MRI brain may be indicated for investigation of hypophysitis.

Treatment involves replacement of deficient hormones and perhaps steroids.

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Immunotherapy is establishing itself as standard treatment for several tumours. Doctors can avoid problems of misinterpretation by being aware of immunotherapy side effects.

Less common side effects

These are pneumonitis, nephrotoxicity, neurological side effects such as neuropathies, Guillain-Barre syndrome, myasthenia gravis and autonomic neuropathy, and ophthalmic side effects such as episcleritis and uveitis.

Management

Most irAEs are easily reversible if recognised and treated early. Immunosuppression with corticosteroids is the mainstay treatment – between oral steroids for persistent low grade side effects and hospitalisation for high dose intravenous steroids for more serious irAEs. In cases resistant to corticosteroids more potent immunosuppression is required with drugs such as infliximab, mycophenolate or tacrolimus. ●

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