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abstract

Immune-Related Endocrine Adverse Events from Checkpoint Inhibitors: A Systematic Review of Clinical Outcomes and Management

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Immune-Related Endocrine Adverse Events from Checkpoint Inhibitors: A Systematic Review of Clinical Outcomes and Management

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Introduction: Immune checkpoint inhibitors (ICIs) improve survival across multiple malignancies but frequently trigger immune-related endocrine adverse events (irEA-E), which can be irreversible and under-recognized.

Methodology: A structured review of randomized trials, cohort studies, and meta-analyses published between 2018 and 2025 was conducted to evaluate endocrine toxicities associated with anti-PD-1/PD-L1 and anti-CTLA-4 agents. Reported outcomes included incidence, timing, reversibility, and management strategies.

Results: Thyroid dysfunction (5–20%) was the most frequently reported endocrine toxicity, followed by hypophysitis (1–15%), adrenal insufficiency (0.5–2%), and autoimmune diabetes (0.2–1.5%). Onset typically occurs weeks tomonths after therapy initiation. Most events are permanent and require long-term hormone replacement. High-dose corticosteroids are generally reserved for mass-effect hypophysitis or systemic grade ≥3 immune-related adverse events.

Conclusion: The evaluation of the primary tumor process extent revealed: multifocality in 63 (48%) patients, involvement of neck lymph nodes in 115 (88%), lung metastases in 14 (11%). Adjuvant RIT to ablate residual thyroid tissue and reduce the risk of recurrence were performed at an average 131I activity of 2 GBq (1,1-4 GBq), therapy of lung metastases with 131I 4 GBq (1,83-5 GBq). Out of 14 patients with lung metastases, 3 patients had a radioiodine refractory process. Lung metastases were associated with an advanced primary process (T3-4, N1b) and high TTG-stimulated thyroglobulin levels (from 118 ng/ml to >5,000 ng/ml).

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