

Immunotherapy-Induced Endocrinopathies And Their Management In Cancer Patients A Prospective Observational Study

Sadaf Chiragh¹, Khalid Usman², Arif Mumtaz³, Naseeb Urrehman⁴, Salman Kundi⁵

1. Associate professor, Department of Oncology, Hayatabad medical complex, Peshawar.
2. Associate professor, Department of Diabetes and Endocrinology, Hayatabad medical complex, Peshawar.
3. Assistant Professor, Department of medicine, KMU institute medical sciences Kohat.
4. Associate professor of medicine, Khlifa Gulnawaz teaching hospital, Bannu.
5. Associate professor of medicine, DHQ teaching hospital Dera Ismail Khan.

Corresponding Author: Khalid Usman

Associate professor, Department of Diabetes and Endocrinology, Hayatabad medical complex, Peshawar.

Email: usmank70@yahoo.com

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Abstract

Background: Immunotherapy has been transformational in cancer care, but here is the catch; it can lead to endocrine disorders that affect hormone balance and patient health.

Methodology: this study investigated the incidence, management, and outcomes of endocrinopathies amongst the cancer patients undergoing immunotherapy.

Study design: A Prospective observational study.

Place & Duration of Study: Department of endocrolog hmc Peshawar from jan 2019 to dec 2019

Methods:

The current study monitored twice as many individuals (n=200) under immunotherapy due to immune-related adverse events (irAEs) which affected their endocrine functions. Diagnosis and management of conditions such as thyroiditis, hypophysitis, adrenalitis, and diabetes mellitus were conducted using biochemical tests which included hormone levels, and imaging techniques including MRI or CT scans. Patients were provided with individualized treatments by a team consisting of multiple specialists.

Results:

Among the 200 participants, 45 (22.5%) developed an endocrinopathy most of which were thyroiditis. With this technique, a total of 88.9% of patients regained their illness status and continued with cancer chemotherapy regimens. This measure improved standard of living in major ways by effectively managing the associated disorders of endocrine system and as well as preserving therapy efficacy for neoplastic diseases.

Conclusion: our monitoring and interdisciplinary management, Cancer patients can maintain normal hormones through immunotherapy-induced endocrinopathies while staying on treatment protocol.

Keywords: Immunotherapy, Endocrinopathies, Cancer, Management, Outcomes.

Introduction

Cancer care has changed a lot with immunotherapy as well as for patients suffering from advanced cancer it is new hope [1]. This is different from conventional ones like chemotherapy which involves drugs that kill cancer cells or radiation therapy that kills them [2]. Despite its potential, immunotherapy has limitations such as immune-related adverse events (irAEs) [3]. Of particular interest are endocrine disorders including thyroiditis, hypophysitis, adrenalitis and diabetes mellitus since they interfere with optimal hormonal level important for individual's health[4]. For instance, successively managing endocrine irAEs require the co-work of multiple medical professionals with diverse specialization. Besides, there is little information about their incidence and control under immunotherapy in cancer patients more so in some subsets. This shortfall will be filled by this research which looks at the occurrence rates, management modes and outcomes of endocrinopathies among persons who have undergone immunotherapy at the Department of Endocrinology HMC Peshawar from January 2019 to December 2019 within one year. Hence this study will estimate how often these secondary diseases come up in recipients of targeted therapies against malignancies; what forms have proved most beneficial so far; what consequences these methods leave behind after they have been implemented[6]. The present study intends to provide useful insights into clinical challenges and therapeutic responses associated with immunotherapy-induced endocrine dysfunctions through systematic monitoring of two hundred cases[8]. Therefore understanding prevalence and treatment methods for such types of cardiotoxicity may contribute towards improving patient care reducing its detrimental effects as well as maximizing benefits obtained from this modality [9-10] This work also emphasizes the need for alertness coupled with multidisciplinary treatment plans aimed at unraveling complexities existing between cancer treatments and imbalances related with hormones that are experienced by patients [11-12]. These findings will benefit current medical practices and inform future studies on how best to manage endocrine irAEs in cancer patients [13].

Methods

two hundred cancer patients who were undergoing immunotherapy were monitored prospectively for endocrine adverse events at Hayatabad Medical Complex Peshawar. For the diagnosis of conditions such as thyroiditis, hypophysitis, adrenalitis and diabetes mellitus, biochemical tests including hormone assessment and imaging modalities like Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans were done. From an integrated care team, patients received personalized therapies.

Inclusion Criteria

Patients on immunotherapy for cancer treatment from January 2019 up to December 2019.

Exclusion Criteria

Patients with preexistent endorphin disorders or those not on immunotherapy.

Data Collection

Data was collected through medical records, biochemical test results and imaging studies that documented incidence and management of endocrine irAEs.

Statistical Analysis

The Statistical Package for Social Sciences version 27.0 was used for statistical analysis. Demographic mean indicated patient demographics while chis square evaluated the relationship between endocrinopathies and patient outcome at <0.05 level of significance.

Results

Of the total number of 200 patients, 45 (22.5%) developed endocrinopathies. Twenty out of those that had been affected by this condition were diagnosed with thyroiditis (44.4%). Hypophysitis was noticed in ten subjects (22.2%), adrenalitis – eight cases (17.8%), diabetes mellitus- seven instances(15/6%). This number includes forty patients who continued their anticancer therapy due to durability maintained through multidisciplinary care practice that delivered stable disease control whereas five children received discontinuation because of severe hormonal disorders.

Table 1: Patient Demographics

Characteristic	Number (n=200)	Percentage (%)
Age (years)		
<40	30	15.0
40-59	120	60.0
≥60	50	25.0
Gender		
Male	110	55.0
Female	90	45.0
Type of Cancer		
Lung Cancer	50	25.0
Melanoma	40	20.0
Renal Cell Carcinoma	30	15.0
Hodgkin's Lymphoma	20	10.0
Other	60	30.0

Table 2: Types of Endocrinopathies Observed

Endocrinopathy	Number (n=45)	Percentage (%)
Thyroiditis	20	44.4
Hypophysitis	10	22.2
Adrenalitis	8	17.8
Diabetes Mellitus	7	15.6

Table 3: Diagnostic Methods Used

Diagnostic Method	Number of Patients	Percentage (%)
Biochemical Tests	45	100.0
MRI	25	55.6
CT Scan	20	44.4

Table 4: Management Approaches

Management Approach	Number (n=45)	Percentage (%)
Hormone Replacement Therapy	25	55.6
Corticosteroids	10	22.2
Insulin Therapy	7	15.6
Combined Approach	3	6.6

Table 5: Outcomes of Management

Outcome	Number (n=45)	Percentage (%)
Stable Disease Control	40	88.9
Discontinued Cancer Treatment	5	11.1
Improved Quality of Life	40	88.9

Discussion

Despite the improvements in immune therapies in cancer patients, they still have some flaws like immune-related adverse events (irAEs) which are a clinical challenge. The purpose of this study was to investigate the incidence, management and outcomes of endocrine irAEs in cancer patients receiving immunotherapy at HMC Peshawar. These include Hypophysitis 7 cases (31.8%), Thyroiditis 6 cases (27.3%), Adrenalitis 4 cases (18.2%) and Diabetes Mellitus 3 cases (13.6%). These results concur with existing literature that has also shown the thyroid gland as a common area of immune related injury. This finding show that there is a need for routine monitoring of endocrine functions during immunotherapy [17]. A multidisciplinary approach involving endocrinologists, oncologists, and other specialists was necessary to manage these hormonal disorders. Moreover, hormone replacement therapy was used for managing hypophysitis and thyroiditis while adrenalitis required corticosteroids; insulin therapy was used for diabetes mellitus [9]. An important outcome from this study revealed that under appropriate management, 88.9% of patients had stable disease allowing them continue their cancer treatment. In order to mitigate the burden associated with endocrinopathies on both health status and continuity of cancer treatment, timely diagnosis and comprehensive management should be ensured [19]. The success rate implies effectiveness of a holistic approach to management irAEs', including those affecting the endocrine system. Regular monitoring is also stressed here. There were improved quality of life among patients who attained stable disease control hence able to continue with their cancer therapy uninterrupted. The benefits detected by this research corresponded with existing studies that have recognized early identification as well as prompt medical help vital in dealing with irAEs. What's more however is that according to this study severe endocrinopathies lead to cessation of treatment in 11% of all involved patients with cancer. Thus, there is a need of further research to identify more efficient management protocols as well as possible preventive strategies that will reduce the incidence and severity of these irAEs. In addition, standardized guidelines should be developed by clinicians on how to monitor these adverse effects in immunotherapy [21].

Limitations

The limitations of the study include small sample size and single-center design in which the results may not be generalized. Furthermore, long-term outcomes were overlooked because the study only covered one year.

Future Directions

Future research should comprise larger multi-centre cohorts for the confirmation of these findings. Moreover, there should be studies looking into bio-markers that can enable early diagnosis of endocrine irAEs and also examine strategies for long-term management that may improve patient outcomes.

Conclusion

Management of immunotherapy-induced endocrinopathies requires striking a balance between cancer treatment continuation and maintenance of good health. These findings highlight the significance of vigilant monitoring and inter-professional care for handling such intricate conditions.

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Authors Contribution

Sadaf Chiragh¹ .Concept & Design of Study

Khalid Usman² .Drafting

Salman Kundi⁵·Arif Mumtaz³.Data Analysis

Naseeb Urrehman⁴ . Critical review

Sadaf Chiragh¹ , Khalid Usman² Final Approval of version

References:

1. Postow, M. A., Sidlow, R., & Hellmann, M. D. (2018). Immune-related adverse events associated with immune checkpoint blockade. *New England Journal of Medicine*, 378(2), 158-168.
2. Barroso-Sousa, R., Barry, W. T., Garrido-Castro, A. C., Hodi, F. S., Min, L., & Krop, I. E. (2018). Incidence of endocrine dysfunction following the use of different immune checkpoint inhibitor regimens: a systematic review and meta-analysis. *JAMA Oncology*, 4(2), 173-182.
3. Torino, F., Barnabei, A., De Vecchis, L., Salvatori, R., & Corsello, S. M. (2013). Endocrine side-effects of anti-cancer drugs: mAbs and pituitary dysfunction: clinical evidence and pathogenic hypotheses. *European Journal of Endocrinology*, 169(6), R153-R164.
4. Byun, D. J., Wolchok, J. D., Rosenberg, L. M., & Girotra, M. (2017). Cancer immunotherapy—immune checkpoint blockade and associated endocrinopathies. *Nature Reviews Endocrinology*, 13(4), 195-207.
5. Brahmer, J. R., Lacchetti, C., & Thompson, J. A. (2018). Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology clinical practice guideline summary. *Journal of Oncology Practice*, 14(4), 247-249.
6. Ryder, M., Callahan, M., Postow, M. A., Wolchok, J., & Fagin, J. A. (2014). Endocrine-related adverse events following ipilimumab in patients with advanced melanoma: a comprehensive retrospective review from a single institution. *Endocrine-Related Cancer*, 21(2), 371-381.
7. Faje, A. T. (2016). Endocrinology in the time of immune checkpoint inhibitors. *The Journal of Clinical Endocrinology & Metabolism*, 101(2), 359-361.
8. Cukier, P., Santini, F. C., Scaranti, M., & Hoff, A. O. (2017). Endocrine side effects of cancer immunotherapy. *Endocrinology and Metabolism Clinics*, 46(3), 645-657.
9. Joshi, M. N., Whitelaw, B. C., Palomar, M. T., Wu, Y., Carroll, P. V., & Cudlip, S. (2016). Immune checkpoint inhibitor-related hypophysitis and endocrine dysfunction: clinical review. *Clinical Endocrinology*, 85(3), 331-339.
10. Min, L., Hodi, F. S., & Giobbie-Hurder, A. (2015). Systemic high-dose corticosteroid treatment in managing immune-mediated adverse events associated with ipilimumab in advanced melanoma patients. *Journal of Clinical Oncology*, 33(28), 3193-3198.
11. Weber, J. S., Kahler, K. C., & Hauschild, A. (2012). Management of immune-related adverse events and kinetics of response with ipilimumab. *Journal of Clinical Oncology*, 30(21), 2691-2697.
12. Torino, F., Barnabei, A., De Vecchis, L., Di Vito, L., & Fiorelli, G. (2014). Thyroid dysfunction as an unintended side effect of anticancer drugs. *Thyroid*, 24(9), 1367-1382.
13. Chang, L. S., Zhang, Y., & Jyothula, S. S. (2016). Immune checkpoint inhibitors and thyroid dysfunction: a case series and literature review. *Oncology*, 91(1), 85-88.
14. Blansfield, J. A., Beck, K. E., Tran, K., Yang, J. C., Hughes, M. S., & Kammula, U. S. (2005). Cytotoxic T-lymphocyte-associated antigen-4 blockage can induce autoimmune hypophysitis in patients with metastatic melanoma and renal cancer. *Journal of Immunotherapy*, 28(6), 593-598.
15. Orlov, S., Salari, F., Kashat, L., & Walfish, P. G. (2015). Induction of painless thyroiditis in patients treated with programmed death 1 receptor immune checkpoint inhibitors. *Thyroid*, 25(12), 1331-1334.
16. Eigentler, T. K., Hassel, J. C., Berking, C., Aberle, J., Bachmann, O., & Grünwald, V. (2016). Diagnosis, monitoring, and management of immune-related adverse drug reactions from immunotherapy. *EJC Supplements*, 14, 119-145.
17. Puzanov, I., Diab, A., Abdallah, K., Bingham, C. O., Brogdon, C., & Dadu, R. (2017). Managing toxicities associated with immune checkpoint inhibitors: consensus recommendations from the Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group. *Journal for ImmunoTherapy of Cancer*, 5(1), 95.
18. Tanaka, R., Okiyama, N., & Okune, M. (2017). Immune-related adverse events of anti-PD-1/PD-L1 therapy for melanoma: a mini-review. *Frontiers in Oncology*, 7, 152.
19. Dadu, R., & Hamnvik, O. P. R. (2015). Clinical management of immune-related adverse events in patients treated with immune checkpoint inhibitors. *Annals of Oncology*, 26(12), 2375-2381.
20. Freeman-Keller, M., Kim, Y., Cronin, H., Richards, A., Gibney, G., & Weber, J. S. (2016). Nivolumab in resected and unresectable metastatic melanoma: characteristics of immune-related adverse events and association with outcomes. *Clinical Cancer Research*, 22(4), 886-894.