

SAT-491**Introduction**

The immune checkpoint-blocking antibody nivolumab is recognized as having a crucial role in different malignancies by blocking programmed death-1 (PD-1) receptor immune cells. Besides its benefits, nivolumab may cause endocrine immuno-related adverse events (irAEs), including thyroid dysfunction (TD).

Clinical case

A 71-year-old man, with an uneventful past medical history, was diagnosed with stage IIIB (T4N2M0), epithelial-growth-factor-receptor (EGFR) wild type, lung adenocarcinoma.

The patient underwent 4 cycles of first line chemotherapy with cisplatin/vinorelbine and then radiotherapy, obtaining a partial response.

After 4 months, tumor progression was identified, as assessed by whole-body 18-Fluorodeoxyglucose positron emission tomography (FDG-PET) scan, showing pleural and nodal metastasis. Nivolumab, 3 mg/kg every 2 weeks, was started at this point.

While pre-nivolumab thyroid function was normal, 3 months after starting the therapy, a low serum TSH level of 0.04 mUI/mL (0.38-5.33) was found, associated with a normal level of FT4, of 10.8 pmol/L (7.9-14.4). Thyroid antibody (Ab) tests, including TSH-receptor Ab, were negative. At ultrasound examination, thyroid gland parenchyma was normo-echoic, demonstrating an isoechoic thyroid nodule in the right lobe, with regular margins, measuring 14mm diameter. Previous medical history was negative for thyroid disease.

One week after the referred thyroid function tests, nivolumab was discontinued due to progressive disease as assessed by abdominal magnetic resonance, demonstrating right adrenal metastasis and patient started cisplatin/permetrexed chemotherapy. One month after nivolumab suspension, patient had already normalized thyroid tests, with TSH 2.27 mUI/mL and FT4 9.1 pmol/L. More recently (6 months after nivolumab discontinuation), thyroid function tests continued stable, with TSH 1.05 mUI/ml and T4L 9.4 mmol/l. At this point, patient was receiving permetrexed maintenance therapy.

Conclusions

Immune checkpoint molecules as nivolumab, play a crucial role in anti-tumor immunity evasion. Besides its benefits, it may cause irAEs, including TD.

We believe it's essential to perform thyroid function tests at baseline and before the administration of each nivolumab dose, if possible. Additionally, large prospective studies are required in order to assess, the impact of autoimmunity on the development of TD induced by nivolumab, and its potential effect on overall survival and specific cancer survival data.

Thyroid**THYROID DISORDERS CASE REPORTS I*****Methimazole-Induced Neutropenia in Premature Twins with Graves' Disease***

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Introduction: Neonatal Graves' disease (NGD) occurs in approximately 1-5% of infants born to women with Graves' disease. It is caused by trans-placental crossing of thyroid stimulating immunoglobulin (TSI) antibodies during third trimester. Hyperthyroidism during pregnancy can lead to craniosynostosis, goiter, premature bone maturation, developmental delay or even heart failure in the neonate. Neonatal Hyperthyroidism is usually transient and resolves in few weeks. Treatment consists of beta blockers and Methimazole. Studies in adults recommend discontinuing of Methimazole if patients develop neutropenia. However due to lack of alternatives, we present a case of continued use of Methimazole with neutropenia in newborn twins.

Case Report:

33 weeks gestational age mono-chorionic/di-amniotic twins born to a 34-year-old woman with poorly controlled hyperthyroidism. Mother diagnosed with Graves' disease during 2nd trimester with poor control throughout pregnancy. At the time of delivery, maternal TSH was <0.005uIU/mL(0.358-3.74uIU/mL) and FT4 2.18ng/dL(0.76-1.46ng/dL). Antenatal ultrasound at 32 weeks showed homogeneous enlargement of fetal thyroid glands with increased vascularity in both twins. Babies found to have diffuse goiter and exophthalmos at birth. Thyroid tests remained normal for first 3 days of life. By day 3, babies labs showed TSH <0.005uIU/mL, FT4 -8 ug/dL and TSI >700%. Baseline CBC showed ANC of 4.95K/mm³. Babies were started on Methimazole 0.5mg/kg/day and Propranolol 2mg/kg/day. TFTs fluctuated throughout their stay in NICU and they developed neutropenia with ANC 1.23K/mm³ on day 20 of life. Methimazole was initially discontinued then restarted at 0.25 mg/kg/day 3 days later. There is no recommended protocol for restarting Methimazole. Further follow up showed persistent neutropenia despite multiple dose adjustments in Methimazole, including dosing every other day. ANC was maintained around 800-1100K/mm³. At age 2 months, Methimazole was discontinued completely after TSI antibodies decreased to 400%. ANC remained low until 6 months of life, even after discontinuing Methimazole. Both babies ultimately developed central hypothyroidism and were started on l-thyroxine.

Discussion:

NGD can range anywhere from transient hyperthyroidism to persistent central hypothyroidism. Early diagnosis and treatment is crucial to prevent significant morbidity and mortality. Methimazole is the only approved treatment at this age, and management of Methimazole-induced neutropenia has not been established. Adult studies recommend discontinuing Methimazole in context of neutropenia; we took an approach of decreasing dose gradually. Further studies are needed to establish step-wise approach in managing Methimazole-induced neutropenia.

Neuroendocrinology and Pituitary**NEUROENDOCRINOLOGY AND PITUITARY*****The Prevalence of Impulse Control Disorders in Patients with Acromegaly and Prolactinomas Treated with Dopamine Agonists***

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Objective: There is emerging evidence linking dopamine agonist (DA) use with the development of impulse control disorders (ICD) in patients with prolactinomas. On the other hand, no data exist whether DA use in acromegaly is associated with ICD. We aimed to evaluate the prevalence of ICD, psychiatric symptoms in patients with prolactinoma and acromegaly receiving DA in comparison to those with nonfunctioning pituitary adenomas (NFA) and healthy controls (HC).

Material and Method: Forty patients with prolactinoma, 40 patients with acromegaly, 38 patients with NFA and 32 HC were included in this study. All patients and controls included in the study were evaluated with revised version of Minnesota Impulsive Disorders Interview (MIDI-R), Symptom Check List (SCL-90-R) questionnaire, Barratt Impulsiveness Scale (BIS-11), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI). All of the patients with prolactinoma and acromegaly had been receiving cabergoline therapy but patients with NFA had not been receiving cabergoline therapy at the time of the study.

Results: We detected DA associated with ICD in 3 patients (7.5%) with prolactinoma, and 2 patients with acromegaly (5%). All patients' symptoms resolved after either discontinuation of the drug or surgical intervention. There was no significant difference between patients with acromegaly and prolactinoma in terms of ICD prevalence. On the other hand, ICD was not detected in non functional adenoma and HC. There was no correlation between BIS-11 scores and total dose, mean monthly dose and duration of DA.

According to SCL-90-R, obsession and interpersonal sensitivity positivity was significantly higher in patients with prolactinoma than acromegaly ($p: 0.040$, $p: 0.010$, respectively). There was no significant difference between the groups in terms of BAI, BDI and BIS-11's subscales and total scores ($p > 0.005$). Scl-90 somatization and depression positivity was significantly higher in patients with NFA than acromegaly ($p: 0.043$, $p: 0.024$ respectively). Likewise, scl-90 depression, interpersonal sensitivity and additional items subscale positivity was significantly higher in patients with NFA than HC ($p: 0.005$, $p: 0.045$, $p: 0.045$ respectively).

Conclusion: Although DA dose was significantly higher in patients with acromegaly compared to patients with prolactinoma, there was no significant difference in the prevalence of DA -related ICD. We have showed that there was no association between BIS-11 scores and total DA dose, mean monthly DA dose and duration of DA treatment. The higher prevalence of depression, interpersonal sensitivity in patients with NFA in comparison to HC supports the hypothesis the presence of a pituitary adenoma per se might cause a large psychiatric symptom burden.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Pain Is a Major Driver of Quality of Life and Psychoemotional Health in Lipodystrophy Syndromes

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Background Lipodystrophy is a group of heterogeneous syndromes characterized by selective loss of adipose tissue and metabolic abnormalities. The severity of pain and its possible relation to measures of quality of life (QoL) and psychoemotional and metabolic health have never been studied in-depth previously. **Methods** LD-Lync study is an international multi-center study collecting data on the natural history of different lipodystrophy syndromes. We have completed phase 1 of the study where only a single site (University of Michigan) entered data ($n = 79$ patients, M/F: 16/63, mean age: 46.13 ± 14.60 , 56 with familial partial lipodystrophy). In this study, we sought to investigate the relationship of pain perception on QoL, psychoemotional and metabolic aspects of the disease. Brief Pain Inventory (BPI) was used to calculate pain severity (BPI-SS) and pain interference scores (BPI-IS). **Results** From the 77 who completed the questionnaires, 56 (72.73%) patients reported pain at different levels. Out of the 56, 29 (51.79%) patients had moderate/severe pain (BPI-SS ≥ 4). Patients with moderate/severe pain had "more impaired" QoL scores: physical functioning: 20 (15-50) vs. 80 (45-95), $p = 0.002$; limitation to physical health: 0 (0-25) vs. 75 (0-100), $p = 0.002$; energy/fatigue 15 (10-30) vs. 45 (20-60), $p = 0.032$; emotional well-being: 48 (32-60) vs. 72 (48-84), $p = 0.029$; social functioning: 33 (20-38) vs. 58 (35-70), $p = 0.002$; general health: 15 (10-25) vs. 35 (20-55), $p = 0.005$. Severe depression (PHQ-9 > 14) was more frequently detected among patients with moderate/severe pain (63.2% vs. 36.9%, $p = 0.008$). PHQ-9 score measuring depression was positively correlated with BPI-SS ($r = 0.53$, $p < 0.001$), and BPI-IS ($r = 0.63$, $p < 0.001$). Emotional burden score was also higher in patients reporting moderate/severe pain (4.0 (2.6-5.0) vs. 2.7 (1.6-3.3), $p = 0.015$). BPI-SS/BPI-IS scores correlated positively with disease distress ($r = 0.33$, $p < 0.001$, and $r = 0.31$, $p = 0.010$) and GAD7 scores measuring anxiety ($r = 0.52$, $p < 0.001$, and $r = 0.50$, $p < 0.001$). Anxiety (GAD7 > 10) was more prevalent among patients with moderate/severe pain (58.6% vs. 23.4%, $p = 0.002$). The presence of diabetes was associated with higher BPI-SS scores: 3.50 (1.50-5.00) vs. 0 (0-3.25), $p = 0.030$). Also, patients with HbA1c $> 6.5\%$ exhibited higher BPI-SS scores than those with an HbA1c less than 6.5%: 3.38 (1.38-5.00) vs. 1.25 (0-3.50), $p = 0.030$. **Conclusion** Our study reveals a high frequency of pain perception among patients with different types of lipodystrophy. Pain severity contributes