

mcg/dl). CT-guided core needle biopsy of right adrenal gland was consistent with metastatic hepatocellular carcinoma. CT pelvis with contrast re-demonstrated the right adrenal mass now measuring 11.4 x 10 x 10 cm with new enlarged retrocaval lymph node and no focal arterially enhancing lesions. During embolization of adrenal lesion/hepatic angiogram, multiple liver lesions not previously identified were reported with the largest of 2.9cm size and enhancing lesions in the sacrum and bilateral iliac bones; decrease in size of the necrotic right adrenal mass measuring 8.2 x 9.1 x 9.1 cm 1-month post-embolization. Patient following with Oncology.

Conclusion: Unilateral isolated adrenal metastasis from occult hepatocellular carcinoma (HCC) is extremely rare. Adrenal gland is the second most common site of hematogenous spread from HCC after the lung and has been found in up to 8.4% of cases at autopsy. In our case, the adrenal metastasis was the first clinical presentation of HCC with no evident hepatic lesion until 9 months of adrenal finding; few cases have been reported. Fine needle aspiration/needle biopsy of suspected malignancy is useful to detect primary tumor in case of metastatic disease that is silent at this stage. Adrenal metastasis in HCC are seldom treated by surgery as by the time of diagnosis the tumor is usually far advanced and/or patients are poor surgical candidates. This case highlights the importance of suspecting underlying HCC in isolated adrenal mass in a patient with high risk factors.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

The Short-Term Effect of Multiple Kinase Inhibitor (Lenvatinib) on Spermatogenesis in Mice

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Lenvatinib, a multi-kinase inhibitor, is used in the treatment of solid malignancies. Lenvatinib belongs to a family of tyrosine kinase inhibitors and targets VEGF receptors 1-3, FGF receptors 1-4, PDGF receptor alpha, RET and KIT. However, it is not known whether Lenvatinib like other chemotherapeutic drugs affects spermatogenesis. The objective of this study was to examine whether Lenvatinib induces damage to spermatogenesis in mice. Twenty adult mice (C57BL/6) were randomly divided into 2 groups to receive daily gavage of either water (as control) or Lenvatinib (10 mg/kg) for 6 weeks. All mice were euthanized at the end of the study. We identified that Lenvatinib significantly ($p < 0.05$) decreased testis weight (TW: 91.75 ± 1.49 mg) compared to control mice (TW: 111.9 ± 3.07 mg). This difference in testis weight however, became non-significant after correcting for body weight. The cauda epididymal sperm count was significantly ($p < 0.01$) decreased in the Lenvatinib treated (0.82 ± 0.04 million/mg cauda) as compared to control (1.26 ± 0.07 million/mg cauda)

mice. There were no differences in plasma testosterone concentrations between Lenvatinib treated (29.76 ± 7.67 ng/dl) and control (31.72 ± 6.89 ng/dl) mice. Lenvatinib did not induce notable morphological changes in testicular histology. We conclude that 6 weeks of Lenvatinib treatment had minimal effect if any on mouse spermatogenesis. The long-term treatment effect of Lenvatinib on spermatogenesis remains to be determined.

Adrenal

ADRENAL - TUMORS

New Data on High Prevalence and Time of Occurrence of New Onset Hypothyroidism Associated with Mitotane Therapy in a Cohort of Adrenocortical Cancer

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Context. Mitotane is a steroidogenesis inhibitor and an adrenocorticolytic drug used to treat adrenocortical cancer (ACC). Central hypothyroidism is recognized in mitotane-treated patients and recent data suggested that mitotane could have an inhibitory effect on TSH-secreting cells in the pituitary gland. Moreover, mitotane may lead to induction of thyroid hormone metabolism. Clinical data on hypothyroidism related to mitotane such as prevalence and time of occurrence was described in a limited number of patients.

Objective. To better characterize clinically secondary hypothyroidism in patients with ACC treated with mitotane therapy.

Methods. We reviewed retrospectively paper charts and electronic records from patients with histologically confirmed diagnosis of ACC evaluated at our center from 1995-2019. We analysed the pattern of TSH and thyroid function, but also mitotane timing and levels at baseline and during treatment of patients under mitotane therapy. Thyroid hormone assessment including TSH, FT4 and FT3 was performed at least every 3 months during follow-up.

Results. Our cohort of 104 patients with ACC includes 84 patients that received mitotane therapy. Among them, thyroid function data was incomplete for 39 cases. Complete data was retrieved from 45 patients. Ten out of 45 (22.2%) patients were already known for primary hypothyroidism and were receiving L-T4 replacement before the initiation of mitotane. Two of 45 (4.4%) patients maintained a normal thyroid function during complete follow up (4.5 years) and 33/45 (73.3%) had new onset hypothyroidism requiring levothyroxine treatment. Of these 33 patients, 22 were females and 11 were males, ranging from 22-74 yo with a median of 46 yo. The number of patients with ENSAT stage I, II, III and IV of disease were 1, 8, 11 and 13 respectively. Thyroid profiles were compatible with central hypothyroidism (low T4 with low or inappropriately normal TSH) in 22/33 patients (66.7%). Interestingly, 6/33 patients (18.2%) developed a TSH elevation with a normal lower-limit or low T4 level. The timeline distribution of the occurrence of hypothyroidism was 21.2% (n:7) at <3 months, 15.2% (n:5) between 3-6 months, 21.2% (n:7) between

6-9 months and 15.2% (n:5) between 9-12 months. 9.1% (n:3) occurred within the second year of treatment (between 12-24 months). However, in 5/33 (15.2%) cases, the exact time of new hypothyroidism onset was undetermined.

Conclusion. Mitotane therapy is frequently associated with new onset hypothyroidism with a prevalence of 73% in our cohort of exposed patients and is most likely of central etiology. 72.7% of cases occur in the first year of treatment while 9.1% occur in the second year. This study supports the importance of monitoring thyroid function (including a free T4 level) during the complete course of mitotane therapy.

Thyroid

THYROID CANCER CASE REPORTS II

Thyroid Microcarcinoma Histopathology Relevance

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MON-449

INTRODUCTION: Thyroid carcinoma is the most common endocrine neoplasia. The predominant histological variant is the papillary subtype. Tumors with 1 centimeter diameter or less are defined as papillary thyroid microcarcinoma (PTMC). The clinical diagnosis of PTMC is challenging. The evaluation of the gland includes mostly image methods and fine-needle aspiration (FNA). Nevertheless, the sensibility of these techniques, when compared to total thyroid histology, is less than desired. **AIM OF THE STUDY:** Recognize the real prevalence of papillary thyroid microcarcinoma (PTMC) based on histological evaluation of the total gland among a group of adults in Brasilia, Brazil, and compare the data with the clinical suspicion of PTMC established by FNA and ultrasonography (USG). **PATIENTS AND METHODS:** Retrospective cohort study based on medical records of 76 patients who underwent surgical thyroidectomy treatment for several types of thyroid diseases at the University Hospital of Brasilia - Brazil, from 2005 to 2015. A full inclusion of the surgical specimen was made and stained with hematoxylin and eosin. All of the preparations were evaluated by an expert pathologist. The histopathological report was compared to the previous clinical diagnosis, which was based on FNA and USG of the gland. In addition, the exams results were stratified by the Bethesda criteria. **RESULTS:** Seventy-six individuals with the histopathology diagnosis of PTMC were included (68 were females). A total of 65 FNA and 57 USG results were evaluated, 6 patients had only the histopathologic diagnosis of PTMC. A total of 52 patients had both USG and FNA of the thyroid. All of the patients that had USG records had at least one thyroid nodule, 52,6% of them had multiple nodules. Regarding the FNA results, only 9,2% were classified as Bethesda I; 21,5% as Bethesda II; 7,7% Bethesda III; 7,7% Bethesda IV; 10,8% Bethesda V; 43,1% Bethesda VI. At this cohort, 19 patients were false negatives. The sensibility of FNA for diagnosis of PTMC was 67,79%. **CONCLUSION:** Despite careful evaluation of the patients, there might have false negatives results.

Total thyroid total inclusion of surgical specimen is not a routine diagnostic tool, making less invasive new diagnosis methods desirable.

Thyroid

THYROID DISORDERS CASE REPORTS II

Nivolumab Related Primary Hypothyroidism: 3 Years of Follow-Up

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SAT-514

BACKGROUND: Primary hypothyroidism is one of the most common endocrinopathies related to the use of nivolumab, a monoclonal antibody against the immune checkpoint molecule programmed death-1 (PD-1). The long-term course of this condition, especially after the completion of nivolumab treatment, has not been widely reported.

CLINICAL CASE: A 70-year-old man presented with weight gain despite poor appetite, cold intolerance, and constipation. He noticed these symptoms after receiving the first three months of treatment with nivolumab for renal cell carcinoma. His heart rate was 66, blood pressure was 130/79 mm Hg, and body mass index was 28.3. The thyroid gland was normal-sized without palpable nodules, deep tendon reflexes were normal, and cardiac and pulmonary exams were unremarkable. Laboratory test results were consistent with primary hypothyroidism: thyroid-stimulating hormone (TSH) was elevated at 97.11 mIU/L (normal, 0.35-4.70 mIU/L), and total thyroxine was less than 1 mcg/dL (normal, 4.5-12.0 mcg/dL). Both anti-TPO antibody (222.6 IU/ml, normal <5.6 IU/ml) and anti-thyroglobulin antibody (10.6 IU/ml, normal <4.1 IU/ml) levels were elevated. There was no prior history of thyroid disease; two of the patient's sisters had chronic hypothyroidism. Treatment with levothyroxine resulted in rapid resolution of symptoms. With dose titration of levothyroxine over the course of a few months, the patient achieved biochemical euthyroidism. Nivolumab therapy was continued for more than two years, during which a stable levothyroxine dose was maintained, and the patient remained clinically and biochemically euthyroid. Ultimately the renal cell carcinoma was determined to be in remission, and nivolumab therapy was stopped. Subsequently, the anti-TPO antibody titer was observed to have returned to the normal range (2.3 IU/ml). However, as of five months following discontinuation of nivolumab, and 32 months since the onset of thyroid dysfunction, the patient's hypothyroidism persists as reflected by non-suppressed TSH values on levothyroxine treatment. **CONCLUSION:** We have observed the course of nivolumab-induced primary hypothyroidism over almost three years in an individual patient. The hypothyroidism has persisted, requiring ongoing levothyroxine replacement at a dose of approximately 1.4 mcg/kg daily. An interesting feature of this case is the disappearance of anti-TPO antibody positivity after discontinuation of nivolumab. We speculate that the ongoing hypothyroidism despite the absence of detectable autoantibodies may be related to progressive thyroid cell apoptosis. Further long-term observations will determine whether permanence of nivolumab-induced hypothyroidism is the rule.