however, an important subset of these cancers known as the tall cell variant (TCV), portend a more aggressive prognosis. TCV PTC is characterized by cells, which are at least twice as tall as they are wide. Patients diagnosed with TCV PTC fare worse than those with the classic variant. A less common thyroid cancer, spindle cell squamous cell carcinoma (SCSC), may arise as a primary tumor, but rarely also alongside or from a previous TCV PTC (1). It may also occur as a component of an anaplastic thyroid cancer, the most aggressive and rarest thyroid malignancy. There are three main types of anaplastic SCSC arising from TCV PTC based on histological characteristics: Type 1 is defined by the presence of **both** TCV and SCSC within the initial resection; type 2 refers to when the SCSC arises as a recurrence or metastasis in patients with a known history of TCV PTC; type 3 occurs when SCSC presents as a primary laryngeal SCC in patients with or without a known history of TCV. We report a case of type 2 anaplastic SCSC.

Clinical Case: A 76 yr old man with hx of invasive TCV PTC (diagnosed 2011) s/p total thyroidectomy with b/l neck dissection and laryngectomy, as well as 200 mci of I-131 (in 2012), returns to clinic in 2019, with worsening unexplained weight loss (> 20 lbs). He had been lost to follow-up since 2015. Now, chest CT showed a new, necrotic, left lower lobe mass obstructing the bronchus, as well as bony erosion of the right clavicle and manubrium. Bronchoscopy of the mass was performed, and pathology was consistent with metastatic anaplastic thyroid cancer with squamous nests. Immunohistochemistry was positive for PAX-8, p40, p63 and negative for TTF-1, Napsin A, TG and PDL-1. The endobronchial tumor tissue was compared to the prior resection specimen from 2011, showing morphologic similarity to the squamoid nests. In retrospect, these nests likely represented small foci of anaplastic thyroid cancer arising in association with TCV PTC. The positive staining for PAX-8 and lack of expression for TTF-1 and Napsin A supports this interpretation and is evidence against a primary pulmonary squamous cell carcinoma. Next Gen Sequencing was positive for BRAF V600E mutation, which allowed us to offer BRAF inhibitor and MEK inhibitor therapy. Unfortunately, due to patient's non-adherence to therapy and follow-up clinic visits, we are not able to assess his response.

Conclusion: This is a case of the rarely described type 2 anaplastic SCSC and is an example of the very poor prognosis associated with TCV PTC. It is a reminder that this variant of PTC should be treated more aggressively from the time it is first identified on biopsy.

Reference: (1) Gopal PP et al. The variable presentations of anaplastic spindle cell squamous carcinoma associated with tall cell variant of papillary thyroid carcinoma. Thyroid. 2011;21(5):493–499.

Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

A Brute of a Case: Pituitary Apoplexy in a Patient Treated for Chronic Lymphocytic Leukemia with Ibrutinib.

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SUN-280

Background- Patients treated for chronic lymphocytic leukemia are frequently administered ibrutinib. Ibrutinib inhibits Bruton's tyrosine kinase, blocks the B-cell receptor signaling pathway, thereby reducing downstream effects such as proliferation; effectively treating the malignancy. Adverse events such as bleeding have been reported and are suspected to be caused by inhibition of kinases in the platelet aggregation pathway.

Clinical Case- A 60-year-old man with chronic lymphocytic leukemia, treated with ibrutinib for five months, was diagnosed with pituitary apoplexy and consequent panhypopituitarism. He presented with a severe headache one month prior to diagnosis. At this time, a non-contrast head CT was interpreted as unremarkable. On second presentation one month later, studies showed a serum sodium of 116 mmol/L (135-145 mmol/L), glucose of 43 mg/dL (65-179 mg/dL), and blood pressure of 95/52. An MRI brain demonstrated an enlarged pituitary with areas of intrinsic T1 hyperintense signal noted within the sella turcica suggestive of blood products. Serum cortisol rose from 0.3 to 8.9 ug/dL (4.5-22.7 ug/dL) one hour after IV injection of 250 mcg cosyntropin. Paired ACTH was < 5 pg/mL (7.2-63 pg/mL). Hydrocortisone was started and blood pressure, sodium, and glucose normalized. LH was 0.9 mIU/mL (3-10 mIU/mL), FSH was 4.7 mIU/mL (1.6-9.7 mIU/mL), and total testosterone was < 0.7 ng/dL (240-950 ng/dL). TSH was 0.115 uIU/mL (0.6-3-3 uIU/mL) with FT4 of 0.84 ng/dL (0.71-1.4 ng/dL). Prolactin was 2.4 ng/mL (4-18 ng/mL) and IGF-1 Z score was -1.28 (-2.0-2.0). Replacement levothyroxine and testosterone were started. Oncology stopped ibrutinib and switched therapy to rituximab and venetoclax. A pituitary MRI two months later showed significant improvement of the T1 hyperintensity (blood products) and a 1.1 cm adenoma was found. During the entire course of his illness his platelet counts ranged from 275 to 431 10^9/L (150-440 10^9/L). His INR was 1.14 and PT 13.2 sec (10.2-13.2 sec). He has recovered well on hormone replacement.

Discussion- Pituitary apoplexy often has underlying risk factors, including pituitary adenomas and coagulopathies. To our knowledge apoplexy has not been reported in patients taking ibrutinib, though bleeding and platelet dysfunction have been well described. Knowledge of the possible side effects of newer anti-cancer drugs is increasingly important for the endocrinologist.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Expression of Cell Synthesis and Dna Repair Markers in Meningioma Recurrence or Regrowth

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Expression of cell synthesis and DNA repair markers in meningioma recurrence or regrowth

Abstract: Meningiomas correspond to 37% of intracranial tumors and are considered the second most common neoplasm of the central nervous system in adults. Most of them are benign with slow growth pattern, common from the fifth decade, more frequent in women and with high recurrence rates. In tumors, there is a reduction in the efficiency of DNA error repair, allowing the proliferation of tumor cells. In this work, we evaluated the protein expression of markers involved in cell synthesis (cyclin D1) and repair of DNA errors (MUTYH, XPF, and XPG) in meningiomas. To date, this is the first study to use the immunohistochemical technique in the evaluation of these repair proteins, relating them to clinical data, tumor variables and recurrence-regrowth free survival. 85 samples were included in the study, patients with a mean age of 52 + 13.3 years, 68% female, in proportion 2:1. Most cases were classified as grade I (79%), meningothelial subtype (38%) and transitional (25%). Regarding surgery, 59% of the patients underwent total resection. Regarding location, the most common was the peripheral (62.2%). Most tumors (64%) were larger than 3cm, with a mean of 3.6±2cm. The median recurrence-regrowth free survival was 67 months (95% CI:57.8-76.6). According to the Kaplan-Meier curve, the recurrence-regrowth free survival rate was 94.4% at 1 year, 76.6% at 2 years and 64.7% at 3 years and 49.4% at 5 years. Grades II and III were prognostic factors for tumor recurrence-regrowth ($p<0.05$). Cyclin D1 was positive in 92%, 77% in grade I and 23% in grades II and III. A statistically significant relationship was found between cyclin D1 and tumor grade ($p = 0.001$), with higher expression in grade II and III. Repair proteins were expressed in most meningiomas. MUTYH (63.5%), 43.5% in grades I and 20% in grades II and III, with a significant relationship between grades II and III and, expression 10-50% ($p=0.02$). Significant association was observed with MUTYH ($p=0.001$) and XPF ($p=0.019$). XPF and XPG were associated with grades II and III ($p=0.002$ and $p<0.001$) and XPF with size >3cm ($p=0.03$). There was a positive correlation between XPF and XPG ($p= 0.02$) and between MUTYH and XPF ($p=0.003$). XP proteins were related to recurrence-regrowth ($p=0.04$), but not with recurrence-regrowth free survival. Our results demonstrate the activation of repair pathways and increased cell synthesis in grades II and III in meningiomas. Cellular synthesis and DNA repair markers are important tools to broaden knowledge about the biological behavior of meningiomas.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

Left Hip Pseudofracture in a Patient with Refractory Paget Disease of the Bone

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Background

Paget's disease of the Bone (PDB) is a benign condition caused by focal abnormal bone remodeling. It is largely asymptomatic and is often discovered incidentally while investigating an elevated alkaline phosphatase (ALP) or imaging studies.

Diagnosis relies on biochemical screening, ALP, as a first line test. X-rays and radionuclide scans can assist in determining the extent of disease. Bisphosphonates are recommended for the treatment of bone pain associated with PDB. Zoledronic acid is recommended as the bisphosphonate most likely to give a favorable pain response. Treatment aimed at improving symptoms is recommended over a treat-to-target strategy aimed at normalizing total ALP in PDB.

Clinical case

A 51-year-old, non-verbal female presented to the Endocrinology office with her legal guardian for a follow-up regarding Paget's disease of the bone. The patient had a past medical history of mental disability and refractory Paget's disease that was diagnosed 13 years prior in the setting of elevated alkaline phosphatase. At the time of diagnosis bone scan showed involvement of both tibias, pelvis and right femur stress fracture. She also had a right femoral fracture 7 years before the current presentation that was surgically fixed with an intramedullary rod. The patient had undergone 5 yearly infusions of Zoledronic acid with persistent elevated alkaline phosphatase.

During her clinic visit the patient endorsed left non-traumatic hip pain as well as difficulty walking over the last 2 weeks. Vital signs were within normal limits. On physical exam she appeared well developed, no acute distress was noted, normal heart rate, regular rhythm and normal heart sounds. Pulmonary effort was normal, no respiratory distress or abnormal sounds were appreciated. Musculoskeletal exhibited bilateral lower extremity bowing. No skin warmth, bony growths or tenderness on palpation were noted.

Lab work revealed ALP 277 u/l, bone specific alkaline phosphatase 95.9 (8.1 - 31.6), BUN 12 mg/dl, Creatinine 0.66 mg/dl, GFR 90, Calcium 9.0 mg/dl, Vitamin D 23.3 ng/mL.

She had been treating the hip pain with as needed NSAIDs. An X-ray of the left femur was ordered, and the study showed possible acute subcapital minimally displaced femoral neck fracture with minimal impaction in the setting of known Paget's disease. The patient was then contacted and asked to present to the ER emergently for further evaluation and treatment.

Upon arrival to the Emergency Department, an MRI of the left hip was performed, demonstrating extensive Paget's disease with no evidence of acute hip fracture.

Conclusions

It is essential to obtain an urgent x-ray in patients with Paget's disease who presents with localized pain. However as this case demonstrates x-ray findings can be misleading due to underlying structural deformity of the bone and further imaging like CT or MRI may be necessary.