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Background: Insulinomas are rare tumors with an incidence of approximately 4 cases per million person per year. Only 39 cases of pancreatic neuroendocrine tumors have been reported in pregnancy. We report a case of pregnancy protecting the mother from manifesting the symptoms of insulinoma. **Clinical Case:** This case describes a 25-year old female who initially noticed symptoms of generalized weakness and oral tingling sensation in Fall 2018. She became pregnant in March 2019. She noticed an immediate reduction of the intensity of her symptoms during pregnancy. Her pregnancy was uneventful, and she delivered a healthy newborn in November 2019. Two months postpartum, she had worsening symptoms including syncopal episodes, confusion, difficulty ambulating and visual changes that improved with PO intake specifically carbohydrate intake. She was evaluated in March 2020 and labs showed the following: venous glucose 32 mg/dL, C-peptide 1.7 nmol/L, BOHB 0.4 mmol/L, Insulin 6.1 microU/ml, Proinsulin 25.8 pmol/L, IGF-2 354 ng/mL, negative insulin antibodies and negative oral hypoglycemic agent screen. TSH was unremarkable and AM cortisol was 16.1 mcg/dL. She was started on diazoxide twice a day. She underwent MRI of abdomen, which was negative followed by an EUS which was also negative. She had run out of her diazoxide and became severely symptomatic resulting in an ER visit where she was found to be hypoglycemic. Further evaluation was done with a Triple Phase spiral CT which showed a 1 cm arterial enhancing focal lesion within the pancreatic neck compatible with insulinoma. This was further evaluated with EUS FNA which confirmed the diagnosis of insulinoma on pathology. Her chromogranin A was 46.5 ng/mL. She is scheduled for surgical removal of the lesion. **Conclusion:** Pregnancy leads to an increased insulin resistance through hormonal changes with increased expression of placental growth hormone, human placental lactogen and the placental variant of corticotrophin-releasing hormone (via ACTH and cortisol production), TNF-alpha and leptin. These changes that increase the insulin resistance act as a protective mechanism against the detrimental effects of an insulinoma. Pregnancy most likely also delayed the diagnosis of the insulinoma in this patient. Further research is warranted to evaluate the effects of an insulinoma on the mother and fetus. **References:** 1) Lowy AJ, Chisholm DJ. Insulinoma masked by pregnancy. Intern Med J. 2001 Mar;31(2):128-9. doi: 10.1046/j.1445-5994.2001.00017.x. PMID: 11480477.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS

A Case of Renal Cell Carcinoma and Pheochromocytoma Due to Germline Inactivating Mutation in Fumarate Hydratase (FH)

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A 60-year-old female with a history of well-controlled hypertension, prediabetes, status post hysterectomy for fibroids, presented for evaluation of hematuria and unintentional weight loss. She denied palpitations, headaches, tremors, and diaphoresis. Initial CT demonstrated a right renal mass suspicious for renal cell carcinoma and an adrenal mass. Magnetic resonance imaging (MRI) confirmed a hypervascular, right adrenal mass (6.7 x 6 x 5 cm) without loss of signal.
Laboratory Testing: elevated 24-hour urine vanillylmandelic acid (VMA) 17.5 mg/24 h (<6), and urine normetanephrines 2276 ug/24 h (122-676) with normal urine metanephrines 158 ug/24 h (90-315). 24-hour urine free cortisol was normal. The patient underwent a right adrenalectomy and partial nephrectomy. Pathology confirmed a low-grade renal cell carcinoma (RCC) and a 6.8 cm pheochromocytoma (PCC). Genetic analysis revealed an inherited mutation in the fumarate hydratase (*FH*) gene, which is diagnostic of hereditary leiomyomatosis and renal cell cancer (HLRCC). Wildtype *FH* codes for an enzyme that converts fumarate to malate in the mitochondrial Krebs cycle. Inactivating mutations in *FH* trigger the hypoxia pathway by activating hypoxia-inducible factor (HIF) thereby promoting tumor growth and angiogenesis.
In PCC, 30-40% are hereditary and another 40-50% are found to have somatic mutations in 1 of 20 PCC susceptibility genes. Several autosomal dominant heritable syndromes, including Neurofibromatosis type 1 (NF-1), von Hippel-Lindau (VHL), Multiple Endocrine Neoplasia Type 2 (MEN 2), and Paraganglioma Syndromes Types 1–5, have an increased incidence of PCC, most of which modulate hypoxia pathways. *FH* mutations are similarly inherited in an autosomal dominant fashion and cause HLRCC.
HLRCC is associated with 75-80% risk for cutaneous and uterine leiomyomas, and a 10-16% risk for type II papillary renal cell carcinoma. The risk of RCC in patients with *FH* mutations is much greater than in the general population, where the prevalence is ~2% in those who lack the mutation. In one study, *FH* deficiencies attribute between 19-41% of all RCC cases. Rare families with PGL/PCC have also been found to carry this germline *FH* mutation. This *FH* mutation is associated with increased risk of metastasis in patients with PGL/PCC by a similar mechanism of carcinogenesis via the hypoxia pathway. Currently, there are no strict guidelines for surveillance in individuals with HLRCC, however, patients should have a yearly abdominal MRI, skin examination every 2 years, and an annual gynecological evaluation for leiomyosarcoma. Each first-degree relative should be offered genetic testing of the *FH* mutation, as 50% of relatives may carry the gene. This case underscores the importance of genetic workups in patients with PCC, especially if associated with other tumors.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS

A Case Report on Parathyroid Carcinoma - an Extremely Rare Endocrine Malignancy

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Background: Parathyroid carcinoma is an extremely rare endocrine malignancy with a prevalence of &It 1%. It is