injection of insulin using this needle is greater in comparison to traditional needles. Such force and lack of direct visualization may potentially lead to failure of insulin delivery. Such challenges may be more obvious in patients with obesity.

Our case highlights the importance of periodic review of insulin injection technique, particularly when glycemic control is suboptimal, and emphasizes the correct choice of insulin pen needle.

References

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Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Age-Associated Local GH Promotes Colon Neoplasia

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Colon polyp and cancer frequency increase with age, yet little is known about age-related mechanisms underlying development of these neoplasms. Defective DNA damage response and accumulation of unrepaired DNA damage can trigger genomic instability and cellular transformation.

Patients with acromegaly have a higher prevalence of colon polyps and, arguably, colon adenocarcinoma, while those with GH signaling deficiency do not develop cancer. We showed that APC+/- mice that all develop colon adenomas exhibit a significant decrease in the number and volume of colon tumors with deletion of the GH transcription factor Prop1. Further, DNA damage response triggered GH expression in colon cells, and GH, in turn, altered DNA damage repair, resulting in DNA damage accumulation and cell transformation both in vitro and in vivo. These findings prompted us to hypothesize that accumulated DNA damage in aging colon induces local GH, suppressing DNA damage repair and creating a milieu consistent with genomic instability favoring neoplastic development.

In human colon tissue we now show increased expression of γH2AX, a marker of DNA breaks, associated with increased GH transcription (detected by RNA scope) and translation (assessed by immunohistochemistry) as well as GH induction in both human and murine colon after DNA damaging radiotherapy. In vitro studies support these results, showing GH induction in normal human colon epithelial cells, fibroblasts, and 3D human intestinal organoids after DNA damage. Of note, local GH was secreted in the medium, indicating a paracrine effect. Paracrine/autocrine GH expression in these cellular models resulted in suppression of p53, induction of EMT, and attenuation of DNA damage response, and accumulated unrepaired DNA damage in human colon cells and in human intestinal organoids. In vivo, colon cells infected with lentivirus expressing GH generated more metastases than did cells expressing control vector. Co-culturing of human normal colon fibroblasts expressing GH together with normal human colon cells led to increased motility and accumulation of DNA damage as well as increased proliferation of epithelial cells on a gut-on-a-chip microfluidic device, confirming paracrine GH effects. In an in vitro model of aging, culturing human intestinal organoids for up to 2 months resulted in decreased telomere length and increased GH mRNA and protein expression associated with suppressed DNA damage response evident by decreased phosphorylation of ATM and DNA-PKcs, both kinases involved in DNA repair, and DNA damage accumulation assessed by Comet assay. Suppression of GH in these aging organoids led to increased phospho-p53 and reduced DNA damage. Although somatotroph axis endocrine activity decreases with age, local GH induced in response to age-related DNA damage may trigger a "field change," creating a milieu favorable for colon neoplastic development.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES MELLITUS

Importance of Immunosuppressive Therapy for Managing Insulin Resistance Type B

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Importance of Immunosuppressive therapy for Managing Insulin Resistance type B Background: Autoimmune Antibodies against insulin receptors leading to refractory hyperglycemia is known as Type B insulin resistance. In addition to insulin management, immunosuppressive therapy appears to be an essential part for successful management. **Clinical Case:** A 20 year old African American woman with no significant past medical history presented to the Emergency Department with worsening nausea and vomiting for 5 days and shortness of breath. She admitted to polyuria, unintentional weight loss of 15 pounds in the last six months, decreased appetite, and hyper-pigmented rashes mostly on her back. The patient was not on any medications at home. No known drug allergies, no past surgical history. Family history was significant for Grandmother with Type 2 Diabetes Mellitus and Lupus on father's side of family. The patient denied use of alcohol, tobacco, illicit and IV drug use. T: 37.2 °C, HR: 124, RR: 25, BP: 105/74, SpO2: 100%. Weight 45kg. Physical exam significant for Tachycardia but normal rhythm. Initial work up revealed new onset diabetes HbA1c 9.6% and massive pericardial effusion on echocardiogram s/p pericardiocentesis. Due to developing complaints of intermittent cyanosis of fingertips and intermittent joint pain of fingers, Rheumatology work up was ordered and positive for mixed connective tissue disease. Patient was treated with Cellcept 1500 mg BID, Plaquenil Sulfate 300 mg daily, and prednisone 12.5 mg BID. Hospital course